

INVESTIGATION OF CONTACT ALLERGY BY PATCH TESTING WITH DENTAL SERIES

Dissertation Submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

In fulfilment of the regulations for the award of the degree

M.D.

DERMATOLOGY, VENEREOLOGY AND LEPROLOGY



**DEPARTMENT OF DERMATOLOGY, VENEREOLOGY
AND LEPROLOGY**

**PSG INSTITUTE OF MEDICAL SCIENCE AND RESEARCH
THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY
CHENNAI, TAMILNADU**

APRIL 2013

INVESTIGATION OF CONTACT ALLERGY BY PATCH TESTING WITH DENTAL SERIES

In fulfilment of the regulations for the award of the degree

M.D.

DERMATOLOGY, VENEREOLOGY AND LEPROLOGY



GUIDE

**DR.REENA RAI, M.D.
DEPARTMENT OF DERMATOLOGY,
VENEREOLOGY AND LEPROLOGY**

PSG INSTITUTE OF MEDICAL SCIENCE AND RESEARCH

**THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY
CHENNAI, TAMILNADU**

APRIL 2013

CERTIFICATE

This is to certify that the thesis entitled “**INVESTIGATION OF CONTACT ALLERGY BY PATCH TESTING WITH DENTAL SERIES**” is a bona fide work of **Dr. SWETHA SUNNY KURIAN** done under the direct guidance and supervision of **Dr. REENA RAI, MD** in the department of Dermatology, Venereology and Leprology, PSG Institute of Medical Sciences and Research, Coimbatore in fulfilment of the regulations of Dr.MGR Medical university for the award of MD degree in Dermatology, Venereology and Leprology

DR.REENA RAI
Professor
Dept. of DVL

DR.C.R. SRINIVAS
Head of Dept.
Dept. of DVL

DR.RAMALINGAM
Principal

DECLARATION

I hereby declare that this dissertation entitled **INVESTIGATION OF CONTACT ALLERGY BY PATCH TESTING WITH DENTAL SERIES** was prepared by me under the direct guidance and supervision of **Professor REENA RAI, MD**, PSG Institute of Medical Sciences and Research, Coimbatore.

The dissertation is submitted to the Tamil Nadu Dr.MGR Medical University in fulfilment of the University regulation for the award of MD degree in Dermatology, Venereology and Leprology. This dissertation has not been submitted for the award of any other Degree or Diploma

DR.SWETHA SUNNY KURIAN

CERTIFICATE BY THE GUIDE

This is to certify that the thesis entitled “**INVESTIGATION OF CONTACT ALLERGY BY PATCH TESTING WITH DENTAL SERIES**” is a bona fide work of **Dr. SWETHA SUNNY KURIAN** done my direct guidance and supervision in the department of Dermatology, Venereology and Leprology, PSG Institute of Medical Sciences and Research, Coimbatore in fulfilment of the regulations of Dr.MGR Medical University for the award of MD degree in Dermatology, Venereology and Leprology.

DR.REENA RAI
Professor
Dept. of DVL

CONTENTS

1.	INTRODUCTION	-
2.	AIMS AND OBJECTIVES	-
3.	REVIEW OF LITERATURE	-
4.	MATERIAL AND METHODS	-
5.	RESULTS	-
6.	OBSERVATIONS	-
7.	DISCUSSION	-
8.	SUMMARY & CONCLUSION	-
9.	BIBLIOGRAPHY	
10.	ANNEXURES	
	i. ABBREVIATIONS	
	ii. MASTER CHARTS	
	iii. CONSENT FORMS	
	iv. PRO FORMA	
	v. IHEC CLEARENCE	

Acknowledgements

ACKNOWLEDGEMENTS

It is my greatest privilege to have been mentored by some of the foremost minds in Dermatology in our country today. I would like to take this opportunity to recognize the efforts of all of the individuals who have guided, encouraged and supported me in one way or another throughout my endeavors in this course.

Firstly, I would like to express my gratitude to my guide, **Dr. Reena Rai**. Without her meticulous guidance and encouragement, this dissertation would not have been possible. She has constantly goaded me on to achieve nothing short of excellence and her approach to patient care is a stable foundation upon which I can forever rely.

Secondly, I would like to thank **Dr. C R Srinivas** for teaching me to how think out of the box and extend my vision beyond the borders of Dermatology. His passion for the subject and humility are qualities I will strive to achieve in my own life. Words are inadequate to describe the wealth of knowledge he possesses and I am truly honored and blessed to have had the opportunity to be his pupil.

I value the academic input and encouragement given by **Dr. Chembolli Lakshmi** throughout my post graduate course. She has taught me the importance of perseverance which will go a long way in my career.

I would also like to thank **Dr. P Surendran** for stressing the importance of therapeutics in Dermatology and for imparting his clinical experiences with me.

I would be remiss if I did not acknowledge my friends and colleagues for their patience and understanding. I would especially like to thank **Dr. Gayathri Krishnaswamy** for always lending a helping hand without fail and being a reliable shoulder to fall back on, **Dr. Anjana Mohan** for her unwavering support and encouragement and infectious optimism towards life and **Dr. Maria Thomas** for her invaluable words of inspiration and for being my steadfast friend throughout my academic years. I would also like to make special mention of **Dr. Swarnalakshimi** who has helped me wherever language was a barrier.

My appreciation extends out to the faculty, post graduates and students of **Sri Ramakrishna Dental College & Hospital**, Coimbatore for helping me through the initial stages of my study. I would like to make a special mention of **Dr. Devina Rai** for her contribution to my study.

I am also grateful to the Associate Professors, Assistant Professors and Senior Residents of the department of Dermatology for sharing their knowledge and experiences.

I especially appreciate the cooperation of my patients who repeatedly came in for patch test readings. This study is only possible due to their involvement.

I am indebted to two more individuals who have helped construct and mold this dissertation. **Mr. Thirumoorthy** for ensuring that the practical aspects of my results were accurate and **Mrs. Shanthi** for painstakingly correcting the minor details of the final copy.

Finally, I would like to thank my parents, family and friends for being pillars of strength throughout my academic stint. Without them, I could have only hoped to get this far.

ABBREVIATIONS

2-HEMA	2-Hydroxy ethyl methacrylate
ACD	Allergic contact dermatitis
BIS-GMA	Bisphenol A glycidyl methacrylate
BM	Burning Mouth
BMS	Burning Mouth Syndrome
DCR	Dental composite resins
DGEBA	Diglycidylether of bisphenol A
EGDMA	Ethyleneglycol dimethacrylate
LP	Lichen planus
MMA	Methyl methacrylate
OLL	Oral Lichenoid Lesions
TREGDA	Triethylene glycol diacrylate

INTRODUCTION

INTRODUCTION

A variety of dental products are being used for patients undergoing dental treatment. These contain a vast number of allergens such as acrylates and metals which can cause contact allergy.¹ The oral mucosa is constantly exposed to a large number of potential allergens and irritants⁴⁹ so it is worthwhile to test whether these patients have a specific allergy to dental materials especially since most of the sensitizers remain in the oral cavity for extended periods of time. For example, dentures, fillings and crowns all have constituents that can cause allergy.²

Contact allergy to dental materials has a plethora of clinical manifestations which are not uniform so the treating doctor must take a detailed history and examination. The common presentations of contact allergy to dental materials in patients are oral lichenoid lesions, gingivostomatitis, burning mouth, cheilitis, lip/facial swelling and oral ulcers.²

Dental personnel handling the raw materials used for dental products are also at risk of developing allergic contact dermatitis. They usually present with hand dermatitis, facial eruptions or respiratory symptoms.²

Dentists mainly use amalgams and composites as fillings for dental cavities. Dental amalgams are composed of a mixture of metals and it is usually an alloy of mercury, silver, tin, copper and other trace metals. All these are potential allergens to dental personnel and patients.³

Dental composite resin is used to fill dental cavities. This composite resin has to undergo a curing process before it can be used. To produce this resin, the dental personnel mix the specific acrylates with benzoyl peroxide and induce a polymerization process. This dough is then hardened by using heat or light. If this hardening has to occur at room temperature the reaction needs substances called accelerators. Certain other additives called inhibitors are used to prevent unintended spontaneous polymerization. In addition to acrylates, both accelerators and inhibitors can cause sensitization.⁴

Acrylates can penetrate through surgical latex gloves and hence the dental personnel handling these materials are not adequately protected from coming into contact with these allergens. These personnel commonly present with occupational hand dermatitis with complaints of burning or itching of hands.⁵

Studies on patch testing with dental series have been conducted mainly in European countries like Sweden, Finland, Croatia, Czech

Republic and Germany.^{2,6,7,8,9} Studies have also been carried out in Canada and United States.^{10,11} Most of these studies involved a retrospective investigations of files of patients who had undergone patch testing with dental series.

AIMS & OBJECTIVES

AIMS AND OBJECTIVES

The following are the aims and objectives of our study:

- 1) To analyze the results of patch testing patients with oral or cutaneous symptoms with dental series and to correlate it with their clinical features
- 2) To analyze the results of patch testing dental personnel with hand dermatitis with dental series.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The oral mucosa is constantly exposed to a variety of substances that are potential irritants and sensitizers. The materials in dentistry are mainly used for dental fillings and in fixed or replaceable devices and they should have good biocompatibility.⁴⁹

Fillings and prostheses contain a wide variety of metals such as gold, mercury, nickel, beryllium, chromium, cobalt, copper, silver, aluminum, indium, iridium, palladium, platinum, tin and titanium.⁴ Mercury and gold have been reported to be the most common metal allergens in dentistry. They are most commonly known to cause oral lichenoid lesions as well as most other metals.⁴

Chromium, nickel and other metals in metal dentures may produce dermatitis, stomatitis and LP, or lichenoid oral lesions.⁴⁶ Mercury and other metals such as copper, silver and tin are the major constituents of dental amalgams. They are classified as binary, tertiary, quaternary, and so forth according to the number of metals they contain.⁴

Fifty one patients were patch tested in a study by Scalf et al.⁴¹ These patients had lichen planus or lichenoid lesions and they were tested with 12 metal allergens. Forty nine percent reacted to one or more mercury allergens and seventy five percent showed positivity to at least one metal.

In the same study by Scalf et al, 34 Patients had oral disease, with or without cutaneous or genital disease. There were several groups of patients according to their clinical features (For example, cutaneous disease only, cutaneous + genital disease, oral + genital, etc.). All these groups gave positive patch test rates in the range of 75 to 80%. Hundred percent of the patients who had the metals removed from the oral cavity had complete or significant resolution of symptoms. In the group of patients who did not remove the metals (62.5%) showed improvement only a year later.

Allergy to metals can present as oral lichen planus. In a study by Koch and Bahmer⁴⁰ extensive patch testing was done in 5 groups of patients: i) Oral LP next to fillings, ii) Oral LP not associated with fillings, iii) Patients with other oral diseases, iv) Patients with burning mouth syndrome and v) A control group with no oral complaints. 79% of patients in the first group showed sensitivity to inorganic mercury, some

even showed late reactions. 87% of these patients who tested positive to mercury had total or significant clearing after removal of the dental mercury. In the other 116 patients with oral complaints (i.e excluding groups i and v), mercury showed positivity only in seven patients. This would indicate that the other oral complaints may not be due to dental metals.

In the same study, sensitivity to gold was found in seventeen patients. Two patients had the gold in the oral cavity removed and they had healing of the oral lesions. 19 patients and 8 in the control group showed sensitivity to palladium but they were not certain of the relevance of these results. Biopsies taken from the patch test reactions often showed lichenoid appearance on histopathology.

Yiannias and colleagues found that fifty four percent of patients with oral lichenoid lesions had positivity to various metals and other allergens. 17 reacted to at least one metal and out of these, gold showed the most number of positivities (14/17 patients). Three patients reacted to mercury, three to silver and four to nickel. In the same study, one patient had allergy to acrylics in a dental retainer and six patients had sensitivity to cinnamic aldehyde or Myroxylon pereirae, which are flavorings.

In a study by Laeijendecker and colleagues,⁵⁰ four groups of patients were patch tested. Each group had twenty patients and they were divided as such: i) with oral lichenoid lesions adjacent to amalgam dental fillings, ii) with adjacent and spreading lesions, iii) with oral lesions elsewhere in the mouth, and iv) controls with ACD but no lichen planus. All groups with oral complaints showed positivity to one or more mercury allergens with the first group showing significantly more numbers than the others. None of the controls were positive. In the first 2 groups, 76% had complete healing of lesions after removing their amalgam fillings. The rest in this group showed improvement. Of the 2 in group (iii), one patient improved and the other showed no change after removal of filling.

From Israel, a report of 103 patients with various oral symptoms and/or cheilitis found the following patch test positives in the order of most frequency: gold, nickel, mercury, palladium and cobalt. Five patients were also allergic to 2-hydroxy ethyl methacrylate.⁵¹

In a survey of 1,132 dental personnel,⁵² thirty six percent of them had cutaneous complaints which were attributed to their work. Patch tests done on fifty five examined dental technicians lead to the diagnosis of 64% with allergic contact dermatitis and 24% with irritant contact dermatitis. 2-hydroxyethyl methacrylate was the commonest allergen,

followed by ethylene glycol dimethacrylate and methyl methacrylate. In the group of patients with allergic contact dermatitis, fingertip dermatitis was the most common presentation. In the group with irritant dermatitis, dorsal hand eczema was the most common presentation.⁵³

Allergy to Uncured Acrylic Monomers

Dentures are mainly made of acrylic resin. This is produced by mixing the acrylic liquid monomer methyl methacrylate with polymethyl methacrylate powder.³⁰ This resin is polymerized and hardened by heating or by self-curing at room temperature. For these self-curing resins, benzoyl peroxide acts as an inducer for the polymerization of the mixture of liquid monomer and polymethyl powder. This process also requires an activator. Usually there is more residual monomer acrylates in the self-cured resin than in the heat-cured one.⁵³

Acrylates used in dentures are mostly polymerized by heat, but in subsequent repair or relining work the self-curing resin is used. Other than in dentures, self-curing acrylic material is also used in crowns, fillings and temporary bridges. Heat-cured polymer acrylic resins are not known to cause sensitization but acrylic monomer on its own is a potent sensitizer. Sufficient amount of acrylic monomer remains back in the

self-cured part of the denture to cause cutaneous and mucosal lesions in individuals with prior sensitization.⁵³

Dental personnel are frequently exposed to acrylic monomers and they can cause allergic contact eczema. Fingertip eczema is also common in these persons. Hence dental workers are recommended to avoid direct contact with liquid acrylic monomers, self-cured dentures and acrylic teeth. These monomers are known to penetrate through latex gloves. Acrylic resin sealers and adhesives may also produce hand dermatitis in sensitized people.⁵³

Acrylates are difficult substances to patch test with as concentrations necessary for allergic sensitization are almost close to irritant concentrations. They should be used for patch testing with caution as the procedure itself can cause primary sensitization.¹⁸ The vehicle used is petrolatum as it slows down spontaneous polymerization of acrylates as this process is speeded up in aluminum Finn chambers used in patch testings.⁵⁴

Individuals who test positive to acrylates generally have multiple positivities and these have been attributed to cross reactions.¹⁸ However, studies in Finland have shown that certain acrylates can be present as

impurities in patch test substances and this may be the cause of multiple positivities.⁵⁵

One study in Sweden suggested refrigerating methacrylates used for patch testing in polyethylene syringes to prevent their concentrations from declining during storage which causes false results during patch testing.⁵⁶ In an article published by the American contact dermatitis society, acrylates were labeled as ‘Contact allergen of the year’, 2012.¹⁸

DELAYED TYPE HYPERSENSITIVITY

Delayed-type hypersensitivity reaction can cause a variety of oral manifestations. They can either present as localized or diffuse lesions and usually present 24-72 hours after exposure. The allergens causing this type of hypersensitivity are usually from external sources.⁷

Delayed-type hypersensitivity reactions – Pathogenesis⁷

It is also known as type IV hypersensitivity and they are allergic immune reactions that act mainly via T cells (cellular immunity). Delayed hypersensitivity can only occur in persons who have previously come into contact and have become sensitized to the specific antigen.

Contact allergy occurs after the skin or mucosa comes into contact with substances that have small molecular mass and these behave as haptens. These haptens get absorbed through the epidermis and bind to protein carriers. These hapten-protein complexes become immunogenic and are capable of causing type IV hypersensitivity. These complexes then enter Langerhans cells which travel to the regional lymph nodes and present the antigen in combination with their own MHC-II molecules to the CD4⁺ T cells. This stimulates memory T cells. After repeated exposure to the same antigen, the Langerhans cells present them to the memory T cells which are then activated.

These T cells secrete various cytokines like TNF- α and TNF- β which in turn induce the expression of adhesion molecules (E-selectin, ICAM-1 and VCAM-1) on the endothelial cells of dermal blood vessels. This allows extravasations of various cells that infiltrate the surrounding tissues. Initially these cells are neutrophils followed by macrophages and monocytes. CD4⁺ T cells also secrete other cytokines like IL-3 and GM-CSF that enhance macrophage accumulation.

T cells secrete IFN- γ which can stimulate macrophage activation. Enzymes from these macrophages cause tissue damage and necrosis. The cytokines produced by the T cells increase the permeability of the capillaries that leads to edema.

There are reports that show patients with such an allergic tendency also have atopy.⁷

This chain of events is common for the pathogenesis of type IV hypersensitivity in both patients presenting with oral symptoms and dental personnel presenting with hand dermatitis.

ORAL MANIFESTATIONS SEEN IN DENTAL PATIENTS

1) Oral lichenoid lesions (OLL)

Patients with OLLs present with soreness or discomfort in the mouth with or without oral ulcers. Type IV hypersensitivity to mercury and other metals in dental amalgams has been suggested as the cause.¹ Removal of amalgams have been reported to improve and heal the lesions.¹³ OLLs can also be caused by metals in dental prostheses like cobalt and chrome.¹⁴

OLLs due to dental amalgams can either be a type IV hypersensitivity reaction or a toxic reaction. Type IV reaction occurs as a result of accumulation of mercury salts in the oral mucosa and this reaction is seen only in a minority of susceptible people. These patients present with reticular white patches, papules, plaques or ulcers over the

mucosa. Toxic reactions due to dental amalgams are less understood. They also result in OLLs but can be differentiated from contact allergy by a negative patch test.¹⁵

2) Contact Allergic Stomatitis

True allergic contact stomatitis is relatively rare but cases of contact allergy to different materials have been reported.^{7,12} The main causes are nickel sulfate, mercury, gold and others.⁷ These metals are used as alloys in dental amalgam fillings. Prosthetic allergic stomatitis occurs due to contact allergy to materials in dental prostheses like acrylates, denture furnish, metal denture alloys and cobalt-chromium pastes used for denture fixation. The lesions are usually seen over the area where the prostheses come into contact with the tissue. Contact allergic stomatitis can also be caused by composite resin fillings which contain acrylates but this occurs less frequently and the reason will be explained subsequently.

Lesions of stomatitis present as erythema, edema, vesicles, bullae, erosions and ulcerations.⁷

3) Granulomatous stomatitis and cheilitis⁷

It is a rare manifestation as a result of type IV hypersensitivity and involves the connective tissue of the oral mucosa. Only the lower lip is involved commonly with unilateral edema. Inflammatory granulomatous lesions can be present elsewhere like the tongue, gingival and buccal mucosa.

4) Burning mouth syndrome (BMS)¹

Most of the patients with BMS wear dentures and few have iron/folate deficiency or oral candidiasis so care should be taken to rule these out. Although one cases series relates BMS to contact allergy to acrylates,¹⁶ it is generally felt that BMS is not due to allergic causes.¹⁷

Dental personnel handling the raw materials used for dental products are also at risk of developing allergic contact dermatitis.¹ Dentists mainly use amalgams and composites as fillings for dental cavities. Dental amalgams are composed of a mixture of metals and it is usually an alloy of mercury, silver, tin, copper and other trace metals.¹⁵ All these are potential allergens to dental personnel and patients.

Dental composite resin is used to fill dental cavities. This composite resin has to undergo a curing process before it can be used. To produce this resin, the dental personnel mix the specific acrylates with

benzoyl peroxide and induce a polymerization process. This dough is then hardened by using heat or light. If this hardening has to occur at room temperature the reaction needs an accelerator (activator). Certain other additives called inhibitors are used to prevent unintended spontaneous polymerization. In addition to acrylates, both accelerators and inhibitors can cause sensitization. Unpolymerized material that remains back after the curing process can leach out and act as an allergen.^{4,18}

Acrylic dentures also require a similar curing process. Both dental personnel and patients are at risk for ACD to acrylates in dentures. Dentures are produced from acrylic resins that are heat cured and they are known to cause allergic reactions.

In one study 30 patients and 18 dental workers tested positive to acrylates. All of them either tested positive to 2-hydroxyethyl methacrylate (2-HEMA) or bis-GMA and so it was suggested that testing with just these two substances can be used to screen for acrylate allergy.²⁶ In a report from India, two patients with oral lesions reacted to triethyleneglycol dimethacrylate.²⁷

Acrylates can penetrate through surgical latex gloves and hence the dental personnel handling these materials are not adequately protected from coming into contact with these allergens.^{18,22} These personnel commonly present with occupational hand dermatitis with complaints of burning or itching of hands.¹

Survey has shown that dental personnel including dentists and assistants report occupation-related skin complaints. It could be postulated that these persons have to repeatedly wash their hands and are prone to developing irritant contact dermatitis but a possibility of allergic contact dermatitis cannot be ruled out as they are also exposed to various occupational allergens such as acrylates. The same allergens can cause mucosal contact allergy such as gingivitis, stomatitis or cheilitis.²²

ACRYLATES

Acrylates are used in paints and adhesives, dental composite resins, printing inks, artificial nails, and medical devices such as contact lenses, hearing aids, and bone cement for orthopedic endoprostheses. The salts of acrylic or methacrylic acid can be polymerized to form solid plastics.¹⁸

The esters of acrylic acid and methacrylic acid are acrylates and methacrylates respectively. The three most important groups of acrylics are²²:

- Monofunctional acrylics (monomers) – Methyl methacrylate (MMA) and 2-hydroxyethyl methacrylate (2-HEMA)
- Polyfunctional acrylics – Ethylene glycol dimethacrylate (EGDMA) and triethylene glycol diacrylate (TREGDA).
- Acrylated and methacrylated pre-polymers – BIS-GMA and urethane dimethacrylate

Acrylic monomers will link together through their single vinyl group to form long, parallel strands that can be melted and once it is cooled it hardens.

The resulting resins are much more rigid but cannot be melted and must be given their definite shape before hardening occurs. The addition of prepolymers, hybrid molecules such as epoxy or urethane acrylates, will make molding easier.¹⁸

Polymerization, or curing, can occur at room temperature or with heat. This process requires the presence of initiators and accelerators.¹⁹ Nowadays, numerous monomer acrylates, mostly used in dental bonding materials, printing inks, and artificial nails, are polymerized by exposure to UV light with help from a priming photoinitiator.¹⁸

In certain systems, curing can be accomplished with ionizing radiation, in the absence of oxygen (anaerobic sealants), or by exposure to water moisture (cyanoacrylate instant glues).

Polymerized acrylates are inert and are not known to cause irritant or allergic contact dermatitis.¹⁸ The uncured monomers (methacrylates) are strong irritants^{20,21} and are also known to cause contact allergy.¹⁸

MMA is used in dental prostheses and hypersensitivity to it has been reported.²² Many European studies have reported ACD to acrylics in dental personnel.^{23,24}

Acrylics are used mainly in dental prostheses, dental composite resin and dental bonding compounds²²:

PROSTHESES (DENTURES)

Dentures are produced from acrylic resins that are heat-cured. Self-curing acrylics are also available but these are used for repairing and relining.⁴ Heat-cured acrylic dentures are known to cause contact allergy.^{4,30}

During the curing process, when the monomer acrylics and polymers are mixed together at room temperature, benzoyl peroxide initiates this reaction to form a hard solid substance. This is called cold curing. When the mixture is heat-cured, no initiator is required. After cold curing, some of the monomer acrylics can remain unpolymerized and this can induce stomatitis and cheilitis in sensitized people. N,N-dimethyl toluidine is used as an accelerator in this process.⁴

In one study the author reported allergic stomatitis due to heat-cured acrylic dentures with onset of symptoms ranging from 1 week to 4 years.³¹ Acrylic dentures also contain other substances such as pigments, plasticizers and cross-linking agents to prevent crazing (cracking) and an inhibitor like hydroquinone.⁴

Some patients complain of burning sensation a few hours after the use of a denture that has been repaired or relined. These symptoms may be due to solvents used for the procedure such as ethyl/amyl acetate, diethyl carbonate or glycerol triacetate.⁴

Other causes of denture stomatitis should be ruled out such as oral candidiasis, dry mouth syndrome in elderly (where there is decreased salivary flow) and trauma.⁴

Dental personnel are exposed to these materials and are at a greater risk of developing contact allergy to acrylics as they handle uncured monomer acrylics which can penetrate through the latex gloves to cause contact allergy.²²

DENTAL COMPOSITE RESINS (DCR)

DCR Contain substances such as Bisphenol-A and methacrylates. Also contains additives that trigger polymerization at specific times:

- Initiators – benzoyl peroxide
- Activators – tertiary aromatic amines
- Inhibitors – hydroquinone

All these can cause sensitization.²² other chemicals used in the curing process are phthalates, benzoin ethers, ultraviolet stabilizers and anti-oxidants and their derivatives.³²

Once the hardened substance is placed in the oral cavity, it is reported that fifteen to fifty percent of the residual dimethyl acrylates remain unpolymerized. This results in the slow release of the degraded products such as formaldehyde.³³

Methacrylate monomers (methyl methacrylate) and urethane-based dimethacrylates (epoxybispheno resins and ethylene-amino derivatives) are the different monomers used in DCR. These can be cured (polymerized) either by chemicals or by ultraviolet or visible light sources.⁴

Epoxy acrylates are dental composite resins that cause sensitization in dental personnel. These can also cause sensitization in workers in the UV light printing industry.²²

Acrylated urethanes are also used in dental composite resins and can cause allergy.^{22,25} Patients are exposed to uncured monomer acrylics only for a short period of time so they are at a lower risk of developing allergy than dental personnel but even a single exposure can cause

sensitization. Burning mouth syndrome has been reported due to prostheses and bridges that contain acrylics.²²

Cyanoacrylates, MMA and acrylic acid have been known to cause immediate hypersensitivity like contact urticaria, pharyngitis and bronchial asthma.²²

DENTAL BONDING COMPOUNDS

They are used to bond the dentin to the resin that has been applied. Bonding systems contain a primer and an adhesive. The primer is first applied to the dentin and then the adhesive over it. This system is polymerized using a visible light curing unit. The dental restorative material is applied over this. Methyl methacrylate and 2-Hydroxyethyl methacrylate have been known to cause fingertip paresthesia.^{5,22,28}

ACRYLICS AND GLOVES

They penetrate through surgical and PVC gloves. Laminated, multilayered, disposable gloves (Eg.4H-gloves) are available but are costly and have a poor fit. 4H-glove fingertips are available.²²

EPOXY RESIN COMPOUNDS

They are based on aromatic dimethacrylate monomers which are produced by a reaction between diglycidylether of bisphenol A (DGEBA) and methacrylic acids. BIS-GMA is the most commonly used monomer in DCR.²²

DGEBA-based epoxy resin is a strong contact sensitizer. They are also present in adhesives, surface coatings, electrical insulators, the building industry.

Bisphenol A is the raw material used in epoxy and acrylic resins. ACD caused by this material is rare.²²

ACRYLIC RESIN POLYMERIZATION ACTIVATORS AND INHIBITORS

Methylmethacrylate monomer, polymethyl methacrylate powder and benzoyl peroxide are mixed to form acrylic resins. They are then hardened into shape by heating. If this reaction has to occur in room temperature, activators(accelerators) are needed. For example, the tertiary amine N,N-dimethyl-p-toluidine (DMT) and 4-tolyl diethanolamine.²² Benzoyl peroxide is used as a catalyst in this process.

N,N-dimethyl-p-toluidine

Only few reports of contact allergy to this material have been reported. There have been reports of denture sore mouth syndrome with DMT positivity.³⁴ Kaaber et al have reported one skin positivity in 53 denture wearers.³⁵

Benzoyl Peroxide

Used as a catalyst for acrylic and polyester resins. It is also present in acne preparations and baking additives. It is also used in treatment of stasis ulcers.²² Benzoyl peroxide has been known to cause stomatitis and there has been one report of allergic contact dermatitis in personnel manufacturing dental prostheses.²²

Camphoroquinone

It is used as an initiator for visible light-cured dental acrylic composite materials and primers. It has been included in the dental patch testing series because of its wide use in dentistry but reports of it being positive are rare.^{22,47}

Hydroquinone/Methylhydroquinone

They are inhibitors used in the curing process. They are used to prevent unintended spontaneous polymerization in acrylic curing process. Hydroquinone is also present in bleaching creams. It has been known to cause occupational depigmentation in persons developing photographs.

Hydroquinone released from dentures has been known to cause gingivostomatitis.²² One study reported cheilitis and stomatitis caused by hydroquinone in one patient but the patient was also positive to many metals as well.^{4,48}

METALS

Dental amalgam fillings, orthodontic wires/brackets and prostheses have a wide range of metals used in them.

Occupational contact allergy to metals is reported even in dental personnel.

Nickel

Nickel is found in dental braces and one population-based study in Denmark showed that individuals with dental braces before body piercing had less prevalence of nickel allergy. However already sensitized patients can present with cheilitis or stomatitis after application of braces.⁴

van Loon and colleagues demonstrated that patients with patch test proven nickel positivity can have allergic stomatitis induced by placing nickel objects in the mouth. Five patients with nickel sensitivity had small nickel plates attached to a tooth for a week. All of them developed stomatitis and these lesions showed histopathological features of allergic reactions.⁵⁸

A case of generalized eczema was reported by Foussereau and Laugier in a patient after wearing a denture. Patch testing showed strong positivity to nickel and chromium and the patient had symptomatic relief after removal of the denture. There were no oral complaints in this patient.⁵⁹

Allergic contact stomatitis and cheilitis can occur from dental plates used in dental procedures.⁶⁰ Many nickel sensitive individuals have acquired allergic stomatitis and cheilitis by holding between the lips

nickel-plated objects such as needles, pins, bobby pins and metal lipstick holders.⁶¹

Aluminum

It is produced from bauxite ore and is a relatively inert metal. It is used widely in many industries such as in dental materials, utensils, aircraft, electrical conductors etc as pure metal or alloy. Aluminum salts are used in deodorants and antiperspirants and irritant folliculitis has been reported. Aluminum salts are also used in dental ceramics.

Sensitization can occur from injection from aluminum-adsorbed vaccines. Children have been reported to have allergic granulomas and nodules after hepatitis B vaccination.²⁹ Ear drops containing aluminum acetate has been known to cause allergic contact dermatitis.³⁶

An important feature to note is contact allergy to the aluminum used in Finn chambers. This should be suspected if all patches show red infiltrated papular rings.²⁹ Another problem during patch testing is when aluminum in Finn chambers interact with the metal salts that are being tested like mercury salts. Nickel and cobalt can interact as well but since all these metals are usually prepared in petrolatum they usually do not have any practical problems.²⁹

Gold

Gold allergy is relatively common and some studies report prevalence of gold allergy as high as 9.5%.³⁷ Gold allergy has been known to be associated with eyelid dermatitis.^{29, 38} Some patients who test positive to gold are able to wear gold ornaments without any symptoms. The reason for this is postulated that certain cosmetic powders have titanium dioxide which may abrade the jewelry and act as carriers to the face to eventually cause contact dermatitis.³⁹

Gold is known to cause oral lichenoid lesions and lichenoid skin eruptions in patients with gold dental fillings.⁴⁰ In one study, gold was the next most common metal allergen after mercury in patients with oral lichen planus.⁴¹ Most of the patients with gold allergy are female and this is possibly due to them wearing more gold ornaments. Although many of these patients with gold crowns or fillings can have a positive reading for gold, most of them don't have oral symptoms.²⁹

Gold was previously widely used in dental crowns and restorations but is less commonly used now as amalgam fillings are cheaper.⁴ Occupational gold allergy has been reported in electronics and gold-plating industries.²² Gold sodium thiosulfate is used in patch testing and are known to give late readings.⁸ It has also been reported that blood levels of gold is in relation with the amount of gold in the oral cavity.⁴³

Palladium

It is a precious metal which is sometimes used instead of platinum in white gold or other alloys for ornaments. It is commonly used in dental alloys for dental restorations. Used in alloys for dental plates, relays and switching systems, television communications equipment and as a catalyst in white gold, aircraft and ornamental work.²²

Palladium can cause both allergic and irritant contact dermatitis.²⁹ It has been known to cause allergic contact dermatitis in the form of granulomas at sites of ear piercing.⁴⁴ Stomatitis is known to occur in patients with dental treatment containing palladium.²⁹

It has been observed that palladium positivites are commonly noted along with nickel positivites.²² In a study done in Denmark, 7.4% of dental patients were patch test positive to palladium chloride (along with nickel) and 0.5% had palladium mono-sensitization (without nickel).⁴⁵

Copper

Is one of the common constituents of dental amalgam.²² Contact allergy to copper is rare but allergy caused by copper intra-uterine devices has been reported.²⁹ Lichen planus of buccal mucosa and tongue

has been reported in a patient who showed allergy to copper and removal of the copper-containing amalgam had cleared the symptoms.⁴⁶

Mercury

Historically mercury is important as it led to the development of patch testing. When a grey mercurial ointment was repeatedly applied onto the normal skin of a patient who had eczema to the same ointment there were similar skin lesions observed.²⁹

Mercury is a part of dental amalgams. Dental amalgam is an alloy of a mixture of equal parts of liquid mercury and a powder consisting of silver (22–32%), tin (14%), copper (8%), and other trace metals, including zinc.¹⁵

Mercury is also present in thermometers, paints and agricultural chemicals. Amalgams of zinc tin and mercury are used as dental cements. Amalgams of gold, silver/copper and mercury are used for teeth fillings.²²

In a review article on oral lichenoid lesions caused by mercury and dental amalgam it was stated that although mercury has been known to cause oral contact allergy there is little evidence that this has ill effects on the health of the patients and that removal of these amalgams can reduce their symptoms.

Systemic contact dermatitis (Baboon syndrome), exanthem, erythema multiforme and immediate allergy have also been reported.²⁹ There has been controversy over whether mercury vapors from amalgam fillings may cause worsening of diseases like Parkinson's disease, multiple sclerosis, Alzheimer's disease and amyotrophic lateral sclerosis (ALS) but there has been no clear scientific evidence for the same.¹⁵

Silver

Dental amalgam alloys contain metallic silver.¹⁵ Silver nitrate has been used as an antiseptic agent, in photography, silver plating, coloring porcelain and mirror manufacturing.²² Silver salts have been reported to cause localized or generalized argyria.²²

Platinum

It is used in dental wiring, jewelry and photography. It has been rarely reported to cause contact allergy.²⁹ Soluble platinum salts have been known to cause contact urticaria, allergic rhinoconjunctivitis and asthma.²² Platinum in dental wiring are known to cause allergy to patients.⁴

Platinosis is a condition caused by platinum salts and this is mainly seen in people working in the platinum refining industry. They present with pruritus, eczema and urticaria.²⁹

Tin

It is used in dental amalgams, tin-plating industry, soldering alloys and collapsible tubes. Allergic contact dermatitis to tin is rare.²²

MATERIALS AND METHODS

MATERIALS AND METHODS

This was a hospital-based, descriptive study done with 17 patients with symptoms of contact allergy and prior history of dental treatment and 7 dental personnel with complaints of hand dermatitis.

Patch testing was performed on all patients with Chemotechnique Dental Series.

The study was conducted in the department of Dermatology, PSG IMS & R, Coimbatore from January 2012 to December 2012.

The institute ethics committee clearance was obtained.

Informed consent was taken from the patients.

PATIENT SELECTION

INCLUSION CRITERIA

1) General patients

- a. Patient who have history of prior dental treatment such as fillings, prostheses, braces, wires etc ...
- b. Patients who present with clinical features of dental allergy such as cheilitis, stomatitis, oral lichenoid lesions or lichenoid skin eruptions **after** dental treatment.

2) Dental personnel

- a. Those who are occupationally exposed to dental materials
- b. Who present with clinical features of contact allergy such as hand dermatitis or other skin lesions **after** exposure to the dental allergens.

EXCLUSION CRITERIA

- 1) Patients with no history of dental treatment
- 2) Pregnant/ lactating women
- 3) Patients on systemic steroids or immunosuppressives
- 4) Patients with other proven causes of oral lesions or dermatitis such as autoimmune disorders, nutritional and infective causes of oral lesions.

METHODS

DETAILED HISTORY

- a. Nature and duration of symptoms
- b. Type and duration of dental treatment prior to onset of symptoms
- c. Any co-morbid illnesses
- d. Any other causes for the symptoms were ruled out
- e. Detailed drug history

EXAMINATION

- f. Thorough examination of oral cavity was done with proper lighting
- g. Lesions were photographed for documentation with DSLR Nikon D5100 with a ring flash.
- h. Lesions of dental personnel with hand dermatitis were also recorded and photographed similarly.

PATCH TESTING

All patients who fit the criteria were advised patch testing with dental series Chemotechnique (Sweden). Thirty allergens and one control were loaded into Finn chambers that are mounted on Scanpor tapes. Care

was taken to load the allergens in the correct order according to the proforma. The patient's back was cleansed with saline-soaked gauze and allowed to dry. The tapes with the allergens were then applied to the back and secured with micropore tape. The patient's were instructed to keep the area dry and to avoid exercise till the readings were taken. They were asked to return to the OPD after 48, 72 and 96 hours for the patch test readings.

Once the patient returned after 48 hours, the tapes were carefully removed and the squares designating each chamber were marked immediately with a marker pen. A gap of half an hour was allowed to lapse before taking the reading.

The findings were recorded onto the proforma according to the standard guidelines.⁵⁷

INTERPRETATION KEY	
?	<i>Doubtful</i> reaction; faint macular erythema only
+	<i>Weak</i> (nonvesicular) positive reaction; erythema, infiltration, possibly papules
++	<i>Strong</i> (vesicular) positive reaction; erythema, infiltration, papules, vesicles
+++	<i>Extreme</i> positive reaction; bullous reaction
2	<i>Negative</i> reaction
IR	<i>Irritant</i> reaction of different types
NT	<i>Not tested</i>

The following antigens were tested. They are part of the Chemotechnique dental series for patch testing:

1	Methyl methacrylate
2	Triethyleneglycol dimethacrylate
3	Urethane dimethacrylate
4	Ethyleneglycol dimethacrylate
5	BIS-GMA
6	N, N-dimethyl-4-toluidine
7	2-Hydroxy-4-methoxy benzophenone
8	1,4-Butanediol dimethacrylate
9	BIS-MA
10	Potassium dichromate
11	Mercury
12	Cobalt chloride
13	2-Hydroxyethyl methacrylate
14	Goldsodiumthiosulfate
15	Nickel sulfate
16	Eugenol
17	Colophony
18	N-Ethyl-4-toluenesulfonamide
19	Formaldehyde
20	4-Tolyldiethanolamine
21	Copper sulfate
22	Methylhydroquinone
23	Palladium chloride
24	Aluminium chloride hexahydrate
25	Camphoroquinone
26	N,N-Dimethylaminoethyl methacrylate
27	1,6-Hexanediol diacrylate
28	2(2-hydroxy-5-methylphenyl) benzotriazol
29	Tetrahydrofurfuryl methacrylate
30	Tin
31	Control

Once the results were obtained, they were recorded separately for patients and for dental personnel.

RESULTS

Demographic details:

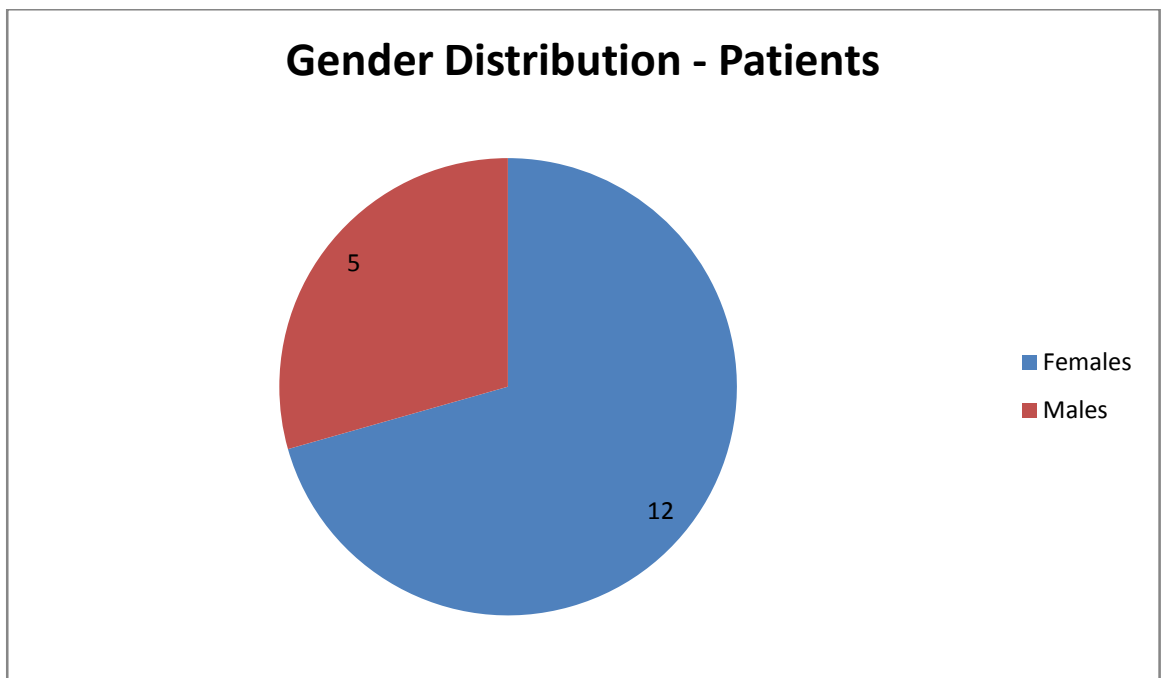


Figure 1. Gender distribution of patients included in study

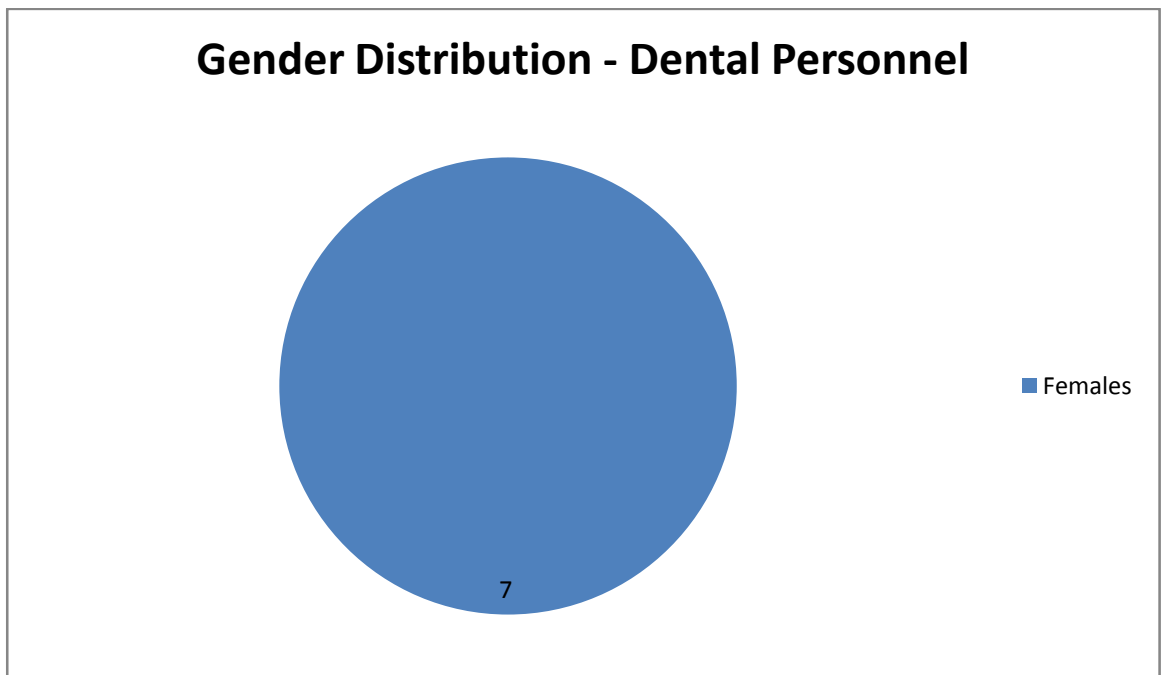


Figure 2. All 7 dental personnel included the study were female.

Age distribution

Group	Age range (years)
Patients	20-55
Dental personnel	20-34

Clinical features – Patients

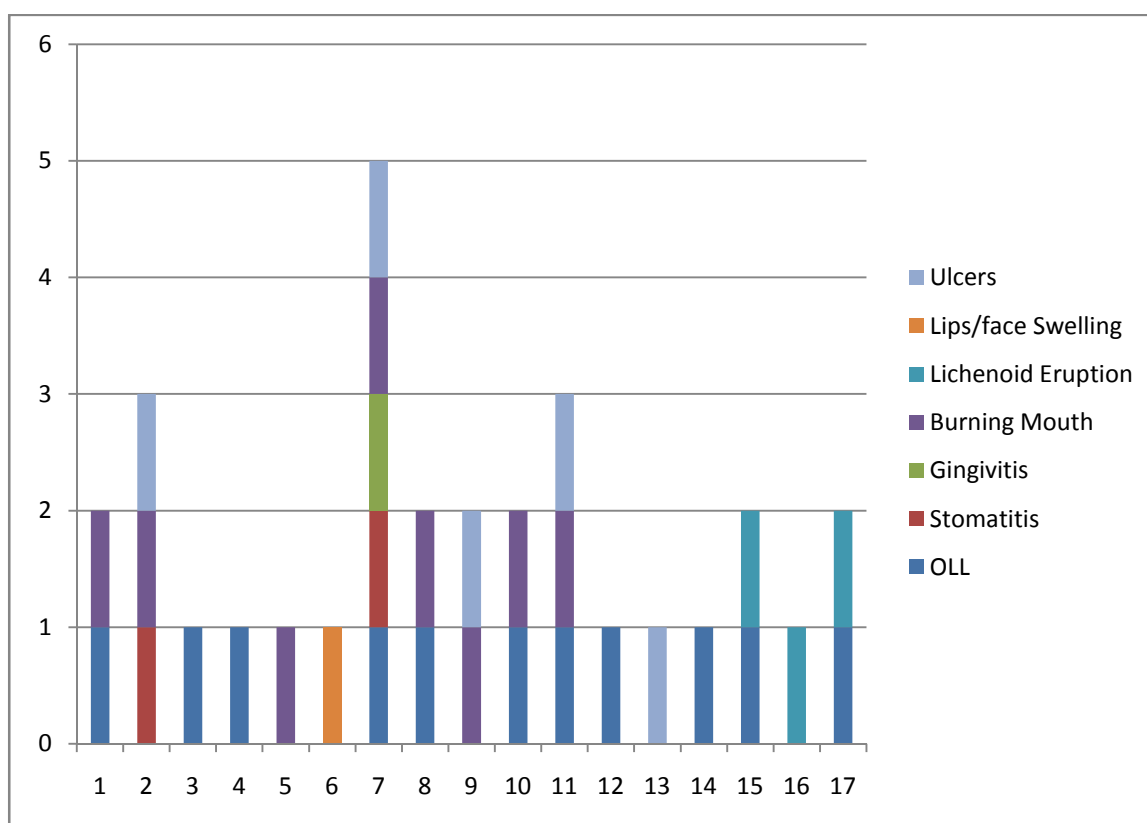


Figure 3. Each patient's individual symptoms have been charted above.

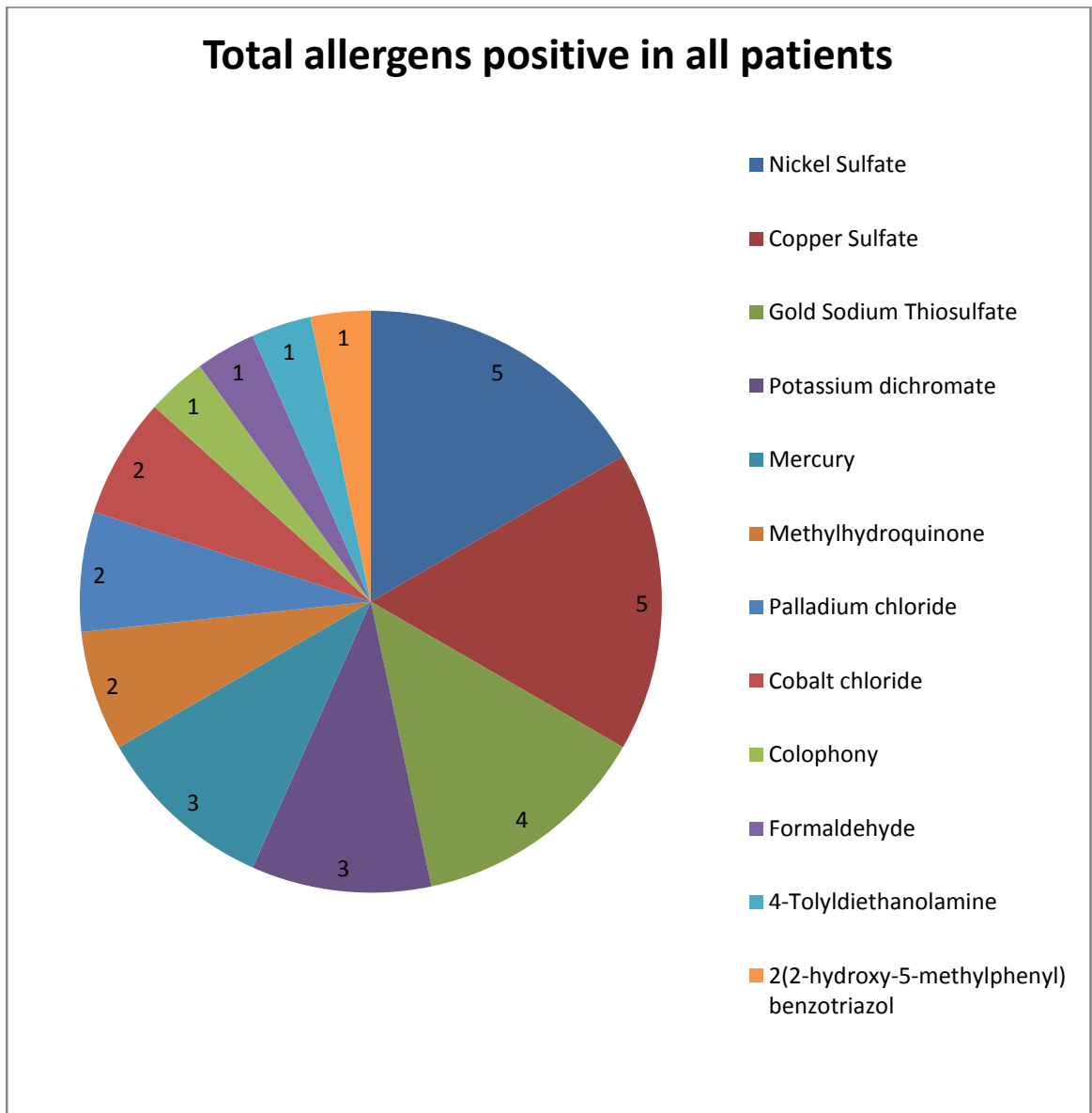


Figure 4 : Total allergens positive in all patients

Most common allergens among patients were nickel, copper, gold and potassium.

None of the patients showed positivity to acrylates.

Positivities according to most common symptoms

1) Oral lichenoid lesions

11 out of 17 patients tested had oral lichenoid lesions (OLL)

6 out of these 11 patients had only single symptom of OLL

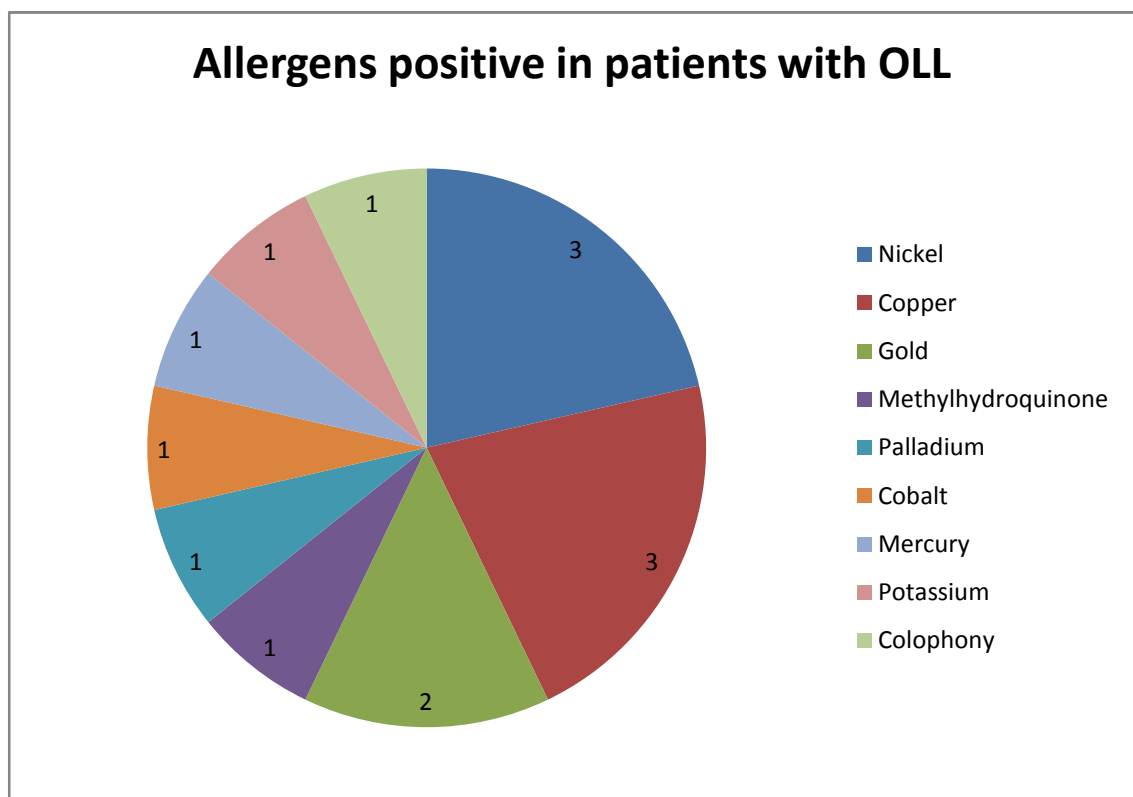


Figure 5 : Allergens positive in patients with OLL

Nickel and copper were the commonest allergens in patients presenting with OLL

Burning Mouth

8 patients had complaints of burning mouth (BM)

Almost all of these patients had other symptoms.

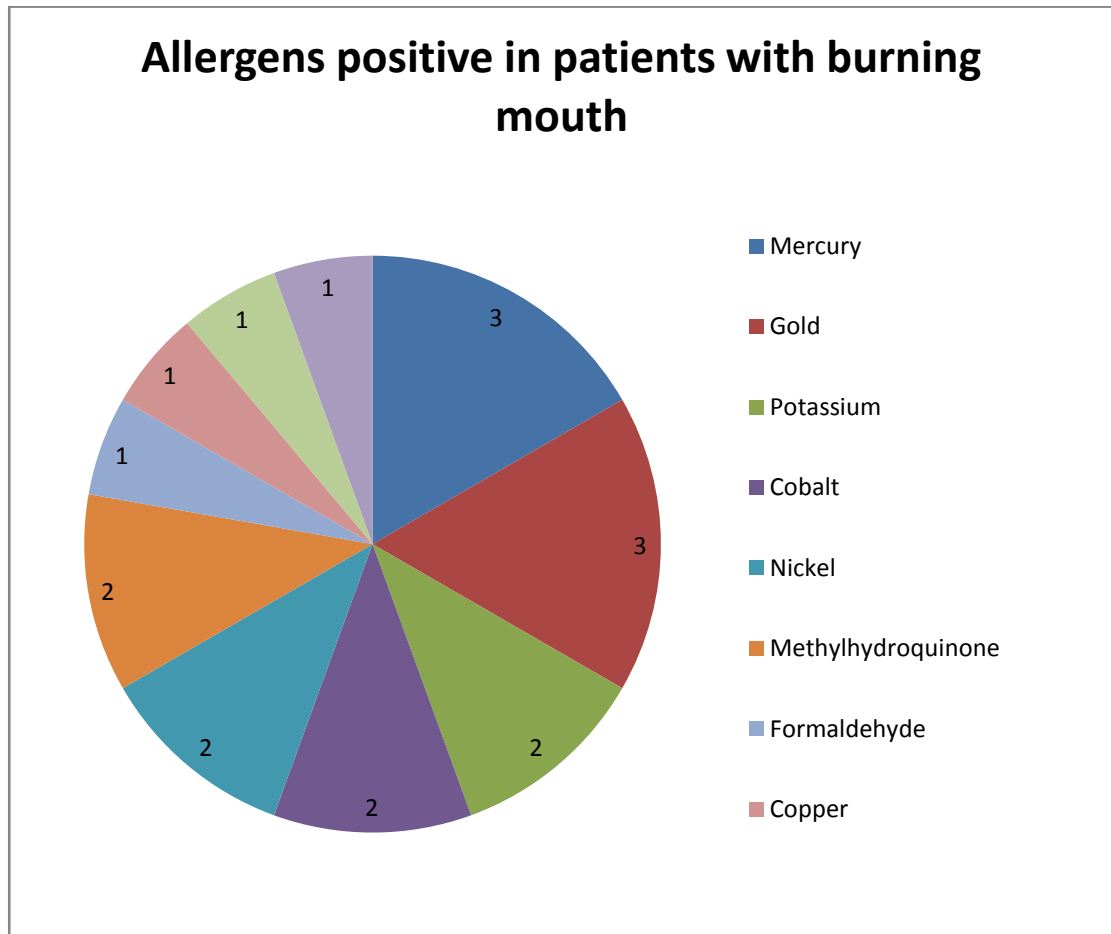


Figure 6 : Allergens positive in patients with burning mouth

The most common allergens in patients with burning mouth were mercury and gold.

Clinical features – Dental personnel

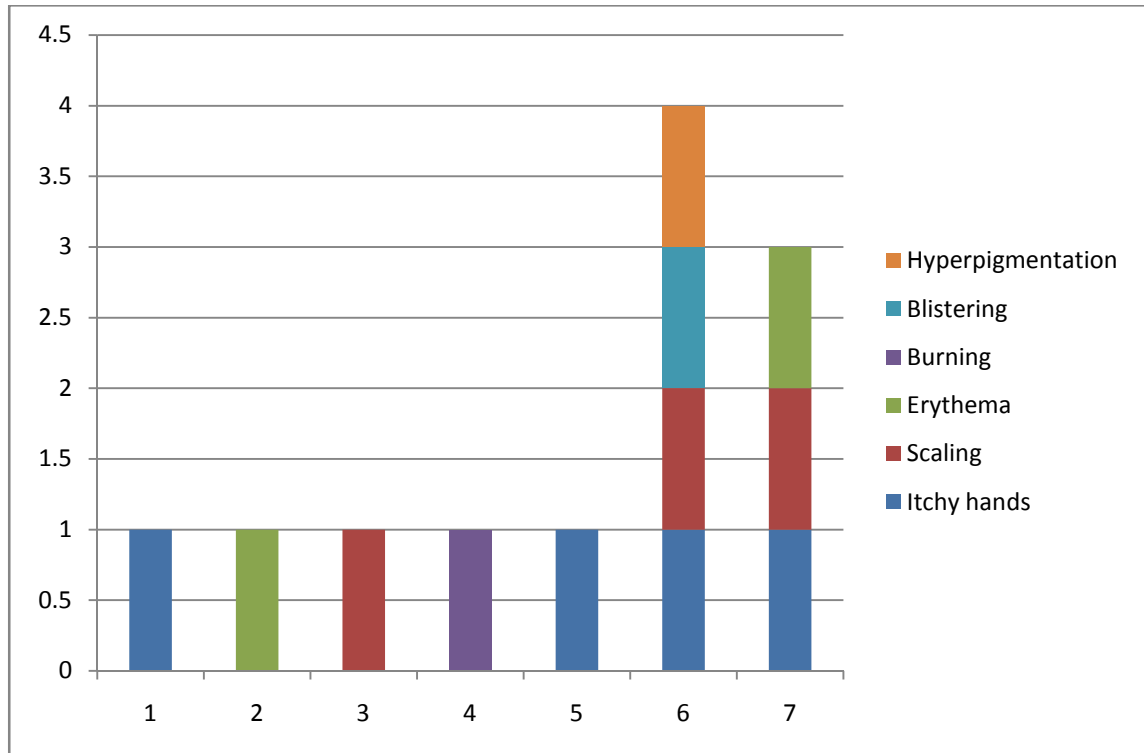


Figure 7. Each dental personnel's individual symptoms have been charted above.

All dental personnel had hand dermatitis with various presentations. Itchy hands was the most common symptom.

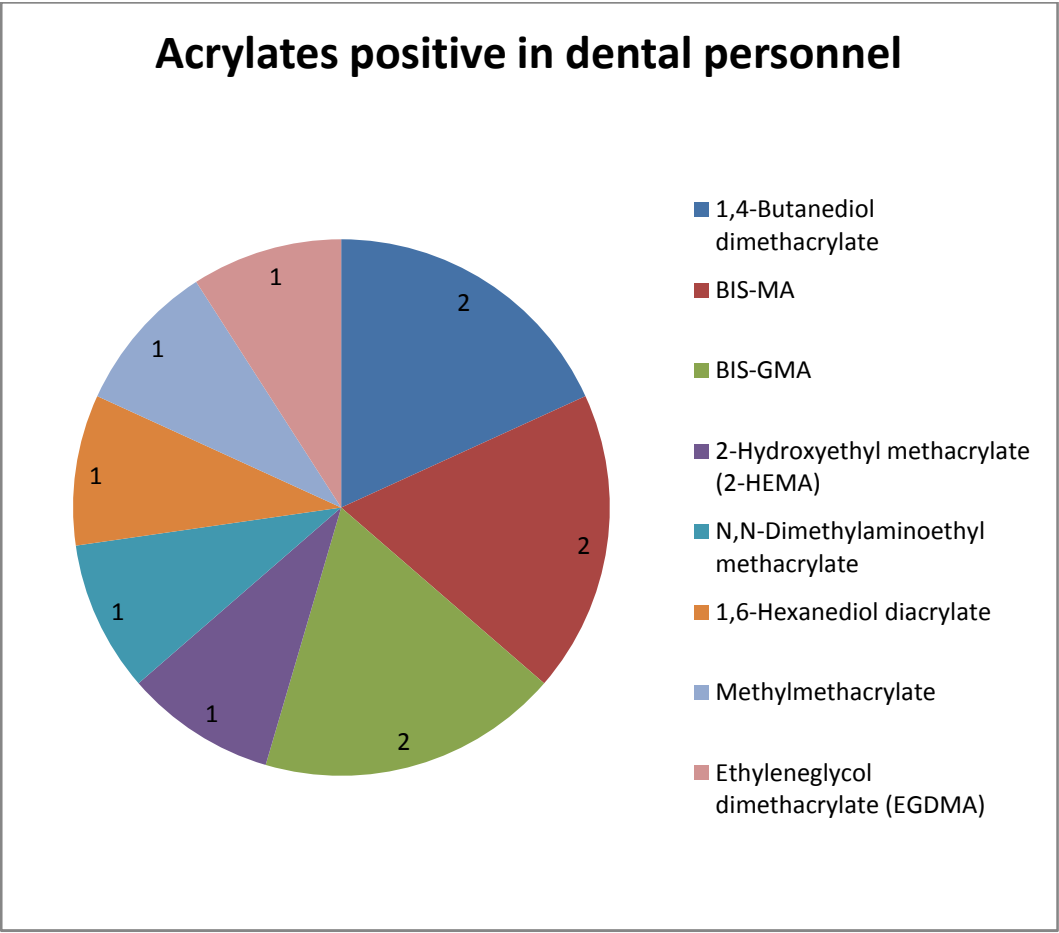


Figure 8. Acrylates positive in dental personnel

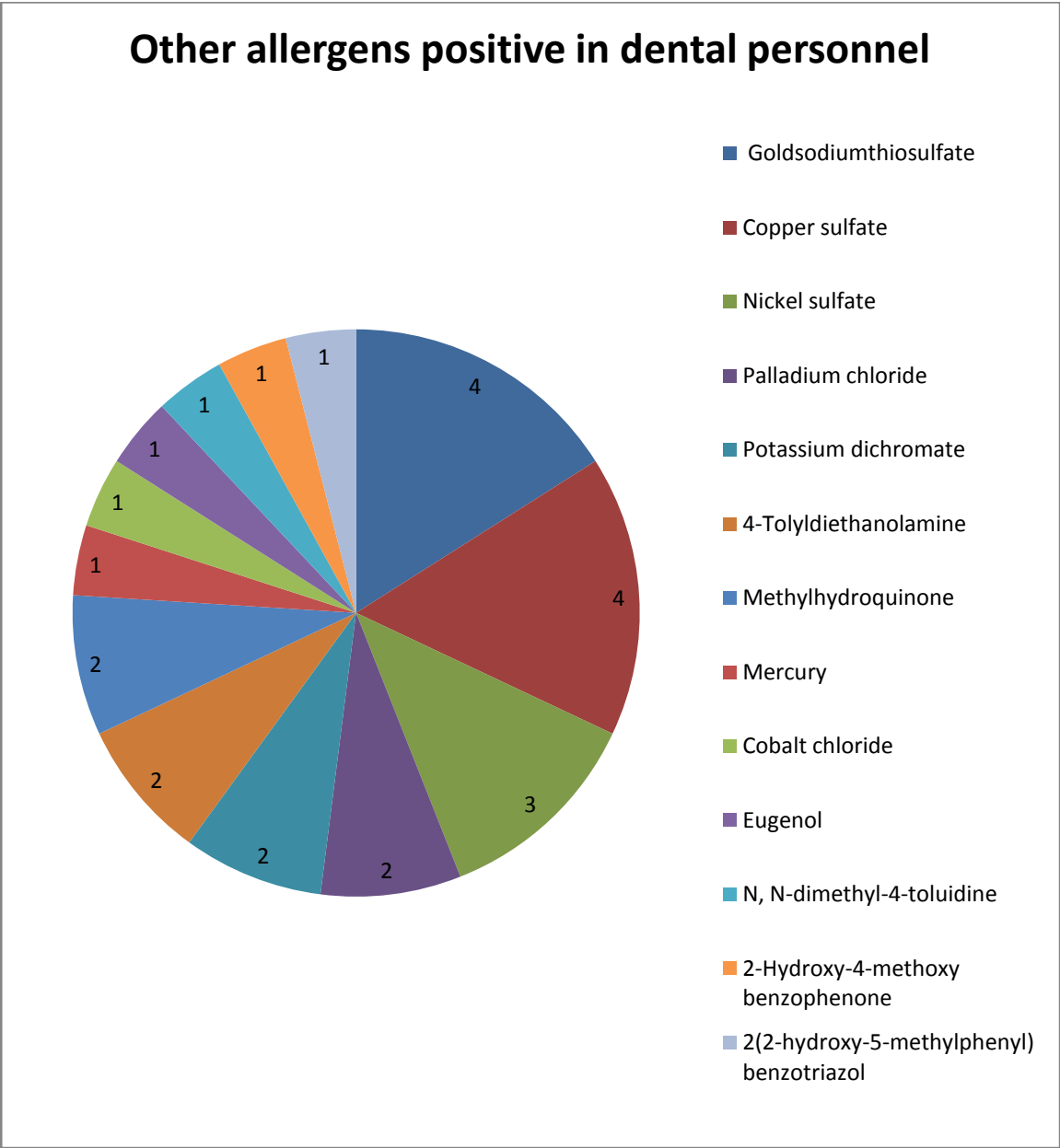


Figure 9. Other allergens positive in dental personnel

Results of patch Testing

17 patients with suspected contact allergy to dental materials were patch tested with dental series consisting of the most commonly used materials in dentistry.

We also patch tested 7 dental personnel with features of hand dermatitis after exposure to dental materials.

Of the 17 patients that were tested, 7 showed no positivity to any of the allergens.

All the dental personnel showed positivity to at least one allergen in the series.

Among the 11 patients who showed positivity, 5 patients showed single positivity the rest 6 showed multiple positivities.

	Total Tested	Nil Positivities	Multiple Positivities	Single Positivity
Patients	17	6/17	6/11	5/11
Dental Personnel	7	0	6	1

DISCUSSION

DISCUSSION

A variety of dental products are being used for patients undergoing dental treatment. These contain a vast number of allergens such as acrylates and metals which can cause contact allergy.¹ Although the oral mucosa is constantly exposed to a large number of potential allergens and irritants, it is worthwhile to assess whether these patients have a specific allergy to dental materials. Especially since most of the sensitizers remain in the oral cavity for extended periods of time.⁹ For example, dentures, fillings and crowns all have constituents that can cause allergy.²

Contact allergy to dental materials has a variety of clinical manifestations which are not uniform so the treating doctor must take a detailed history and examination. Patients should specifically be asked whether the symptoms appeared after the dental treatment. Only then is the association relevant. The common presentations of contact allergy to dental materials in patients are oral lichenoid lesions, gingivostomatitis, burning mouth, cheilitis, lip/facial swelling and oral ulcers.⁷

Metals used in dentistry are the most common causes of ACD in patients as was seen in our patients. Mercury and gold have been implicated as the most common causes of allergy in this setting along with other metals like copper, silver and tin. These are used in dental amalgams and metal dentures.²⁹

Dental amalgams are alloys of mercury and other metals and are used as fillings for tooth cavities. Metal dentures contain nickel, chromium and other metals.¹⁵ All these metals can cause oral lichenoid lesions and other symptoms like dermatitis and stomatitis.²⁹

ACD due to acrylates are less common than metal in patients. Patients are exposed to acrylates present in composite fillings, orthodontic adhesives, root canal sealers, temporary crowns and dentures.⁴

Dental personnel handling the raw materials used for dental products are also at risk of developing allergic contact dermatitis.²² Dentists mainly use amalgams and composites as fillings for dental cavities. Dental amalgams are composed of a mixture of metals and it is usually an alloy of mercury, silver, tin, copper and other trace metals.¹⁵ All these are potential allergens to dental personnel and patients.

Dental composite resin is used to fill dental cavities. This composite resin has to undergo a curing process before it can be used. To produce this resin, the dental personnel mix the specific acrylates with benzoyl peroxide and induce a polymerization process. This dough is then hardened by using heat or light. If this hardening has to occur at room temperature the reaction needs an accelerator (activator). Certain other additives called inhibitors are used to prevent unintended spontaneous polymerization. In addition to acrylates, both accelerators and inhibitors can cause sensitization. Unpolymerized material that remains back after the curing process can leach out and act as an allergen.⁴

Acrylic dentures also require a similar curing process. Both dental personnel and patients are at risk for ACD to acrylates in dentures. In one study 30 patients and 18 dental workers tested positive to acrylates. All of them either tested positive to 2-hydroxyethyl methacrylate (2-HEMA) or bis-GMA and so it was suggested that testing with just these two substances can be used to screen for acrylate allergy.²⁶ In a report from India, two patients with oral lesions reacted to triethyleneglycol dimethacrylate.²⁷

Acrylates can penetrate through surgical latex gloves and hence the dental personnel handling these materials are not adequately protected from coming into contact with these allergens.²² These personnel commonly present with occupational hand dermatitis with complaints of burning or itching of hands.¹⁸

As we suspected type IV hypersensitivity to these allergens, we performed patch tests on the patients and dental personnel. Patch testing is used to detect type IV hypersensitivity to the tested allergens.⁷ The test is performed by applying the allergens onto the skin of the back in specific concentrations within specialized aluminum chambers called Finn chambers.

Studies on patch testing with dental series have been conducted mainly in European countries like Sweden, Finland, Croatia, Czech Republic and Germany.^{2,6,7,8,9} Studies have also been carried out in Canada and United States.^{10,11} Most of these studies involved a retrospective investigations of files of patients who had undergone patch testing with dental series.

In our series of patients with suspected contact allergy whom we have patch tested, 11 out of 17 patients had positive patch tests.

Out of the 11 patients who tested positive, 5 had single positivity and 6 had multiple positivities. We found that the most number of positivities were among the metals.

Nickel sulfate and copper sulfate were the most common allergens with 5/11 patients showing positivity for both.

Nickel

Nickel is very widely used in various applications in dentistry i.e. crown and bridge, partial dentures and orthodontic appliances (wires, bands, brackets).²²

However, hypersensitivity to nickel is most likely from prior sensitization to non-dental sources as nickel is a widely used metal. For example safety pins, watches, belts, artificial jewelry.²⁹

Females have a higher incidence of positivity to nickel, possibly due to greater exposure to the allergen.²⁹ All 5 patients in our study who tested positive to nickel were females and the possibility of prior sensitization to nickel cannot be ruled out.

Commonly reported symptoms of nickel allergy are oral lichenoid lesions, oral oedema, perioral stomatitis, gingivitis, and extraoral manifestations such as eczematous rashes. Nickel is reported to be one of the most common dental metal allergen causing oral lichenoid lesions.²⁹

3/5 of our patients had oral lichenoid lesions. All 5 patients who tested positive for nickel had positivities to other allergens as well (multiple positivities). Four out of the 5 patients who tested positive to nickel had amalgam fillings.

In dentistry, nickel is mainly found in crowns, fixed bridgework, removable dentures, metallic brackets, arch wire bands, springs and ligature wires. None of the patients had any of these devices in the oral cavity and so the positive test to nickel may not be relevant as these patients had tested positive to other metals as well. Only one patient had dental wiring which contains nickel so the patch testing may be relevant in her case.

Nickel is found in dental braces and one population-based study in Denmark showed that individuals with dental braces before body piercing had less prevalence of nickel allergy. However already sensitized patients can present with cheilitis or stomatitis after application of braces.⁴

Patients with nickel sensitivity with a known nickel-containing dental archwire in the oral cavity can be advised to have it replaced with either stainless steel archwire (which has low nickel content) or titanium-molybdenum alloy (which has no nickel). In case the patient has a nickel-containing dental bracket then substitutes are ceramic brackets, polycarbonate brackets and titanium brackets.

Copper

Dental amalgams contain copper but allergic reactions to copper are rarely reported with oral lichenoid lesions.^{22,29,46} However this is not consistent with our findings.

A total of 5 patients tested positive to copper. 4 of the 5 patients with amalgam fillings had positivities to other allergens as well (multiple positivities). 1 patient showed single positivity to copper who had amalgam filling. 1 patient with dental wiring tested positive to copper in addition to other allergens.

4/5 patients who tested positive to copper had metal amalgam fillings (which contained copper) and 1 patient had dental wiring. 4/5 patients had oral lichenoid lesions. One patient had stomatitis, burning

mouth and recurrent oral ulcers. 4 of the patients who tested positive for copper were also positive to nickel.

Although cross-reactions between the two metals have not been reported, nickel is known to be in an impurity in copper patch test substance. Removal of copper-containing amalgams has been reported to clear the lichenoid lesions.²² However none of our patients had their amalgam fillings removed.

Gold sodium thiosulfate

Gold was previously used in dental crowns and amalgams but is not used widely now as dental amalgams are cheaper and more readily available.²⁹

Although gold is known to give late allergic reactions,⁸ (readings should ideally be taken on day 7) our patients showed positivity even within 72 hours.

Patients who have proven allergy to gold are able to wear gold ornaments. It has been postulated that this is because the patients who are symptomatic wear cosmetics that contain microabrasive substances like titanium dioxide. These may abrade the jewelry and act as carriers to cause hypersensitivity.²⁹

Oral lichenoid reactions are known to be the most frequent manifestation of contact allergy to gold.⁸

4/11 patients showed positivity to gold. 3 out of these 4 patients showed multiple positivities and 1 patient was positive only to gold. 2/4 patients had oral lichenoid lesions. They had various other symptoms as well such as oral ulcers, burning mouth and stomatitis.

All the patients who tested positive to gold were females and none of these patients have had any kind of dental treatment done with gold incorporated. This allergy can be due to the fact that they wear gold jewelry.

In one study 34% of patients with gold fillings had positive patch tests to gold as compared to 11% of those patients without gold in the oral cavity.²⁹ In another retrospective study, 30.4% of patients with oral lichenoid lesions had positivity to gold.⁴²

Potassium dichromate

Potassium dichromate is a common inorganic chemical reagent, most commonly used as an oxidizing agent in various laboratory and industrial applications. It is also used to tan leather for footwear, orthopedic and dental implants, green dyes using in felt and textile. Chromium is mainly found in cement.

Three out of 11 patients showed positivity to potassium dichromate. Two out of the three patients had burning mouth and recurrent oral ulcers and one of these patients had stomatitis. One patient had oral lichenoid lesions.

Two patients had amalgam fillings and one patient had dental wiring but none of them had dental implants and so the relevance of positive patch testing to potassium dichromate in our patients could not be established.

Mercury

Mercury is one of the major constituents of dental amalgam. Dental amalgam is an alloy of a mixture of roughly equal parts of liquid mercury and a powder consisting of silver (22–32%), tin (14%), copper (8%), and other trace metals, including zinc.¹⁵

The mercury present in dental amalgam can cause oral lichenoid lesions. This is as a result of type IV hypersensitivity reaction to mercury salts that accumulate in the oral mucosa. However, hypersensitivity to dental amalgam is rare.¹⁵

3/11 patients showed positivity to mercury and all had multiple positivities to other allergens as well. All 3 patients had oral ulcers and burning mouth. One patient had oral lichenoid lesions as well. All three patients had amalgam fillings and one of them also had a composite filling (which contains acrylates). There could be a correlation with their symptoms and mercury allergy.

In many countries the popularity of amalgams is declining due to health concerns. But it is still widely being used because it is inexpensive and durable.¹⁵

According to a 2012 review article on OLL caused by mercury and dental amalgam, although mercury has been known to cause oral contact allergy there is little evidence that this has ill effects on the health of the patients and that removal of these amalgams can reduce their symptoms.¹⁵

In contrast to this, another study by Laine et al in 1997 found that most of the patients with OLL had positive patch test to mercury.⁶² So allergy to mercury should be analyzed with caution.

Palladium chloride

Palladium is used in alloys for dental plates.^{4,29} Two out of 11 patients showed positivity to palladium. Both patients had amalgam fillings. One patient had oral lichenoid lesions. The other patient had stomatitis, burning mouth and oral ulcers

Palladium and nickel are known to cross-react and frequently show concomitant positivity. Both patients who tested positive to palladium also showed nickel positivity. So cross-reactivity cannot be ruled out in our patients.

However, cross reactions between palladium and nickel are not always found²⁹ but in a study done in Denmark, 7.4% of dental patients were patch test positive to palladium chloride (along with nickel) and 0.5% had palladium mono-sensitization (without nickel). This co-positivity between palladium and nickel was also observed in our study.⁴⁵

So the positivity to palladium may not be relevant as none of these patients had undergone treatment with dental plates.

Cobalt Chloride

Cobalt has been used in denture plates and in dental amalgams.⁶³ Generalized eczema has been reported in a patient with a denture plate that contained chromium-cobalt alloy. B Cobalt has been reported to be the most common allergen in children.⁷

2/11 patients showed positivity to cobalt. Both patients had dental amalgam fillings and neither patient had any dentures. One patient showed positivity to other metals but the other was only positive to cobalt. One patient had stomatitis, burning mouth and oral ulcers. The other patient had oral lichenoid lesions and burning mouth.

Methylhydroquinone

It is used as an inhibitor in the curing process of acrylics to prevent undesired spontaneous polymerization of the acrylic monomers.²² 2/11 patients showed positivity. One of these patients had multiple positivities and the other was positive only to methylhydroquinone.

Both patients who tested positive had complaints of burning mouth. Both patients had amalgam fillings but neither had undergone any treatment that composed of acrylics so a correlation between the positive result and clinical features could not be made.

Allergy to methylhydroquinone is not common in patients as they come into contact with the substance for very short periods of time.²²

Colophony

Colophony is a widely used substance in many industries such as the electronic industry, the furniture-making industry, paints and cutting oil. It is also known as rosin. Allergy to colophony in the medical setting has been seen as reactions to sealants in dental prostheses, adhesive skin sutures and adhesive tapes. Colophony causes oral lichenoid lesions.⁶⁴

1/11 patients had positivity to colophony. This patient was 1/6 patients who had multiple positivities. This patient presented with oral lichenoid lesions and had dental wiring treatment done.

Colophony is present in dental prostheses and has been known to cause oral lichenoid lesions.⁶⁴ However our patient did not have any prosthetic treatment and she also tested positive to many allergens. So the positive patch test reading may not have significance in this patient.

Formaldehyde

Formaldehyde is used in antimicrobial dressings during endodontic treatment (root canal treatment). Formocresol is a formaldehyde compound that is used as antimicrobial pastes in root canal dressings. Specific oral lesions have not been described but formaldehyde is a toxic mutagen with carcinogenic potential.⁶⁵

1/11 patients showed positivity but this patient also showed multiple positivities to other allergens as well. The patient had stomatitis, burning mouth and oral ulcers. She had an amalgam filling. As the patient tested positive to many allergens, a clear correlation could not be made for a positive reaction to formaldehyde in this patient.

Dental Personnel

Out of the 7 dental personnel with hand dermatitis only one patient had single positivity and the rest 6 had multiple positivities. One of these personnel had dental wiring done and another had amalgam filling but neither of them had any oral lesions or lichenoid skin lesions and they were tested for their complaints of hand dermatitis.

Gold sodium thiosulfate, copper sulfate and nickel sulfate were the most common allergens with four out of seven positivities each. Allergy to metals along with acrylates in dental personnel has been reported as is seen in our study.

The most common acrylate allergens in our study were BIS-GMA, BIS-MA and 1,4-Butanediol dimethacrylate.

In one study it was concluded that 2-Hydroxyethyl methacrylate (2-HEMA) and bis-GMA could possibly be used to screen for acrylate allergy as they had 100% positivity. This is because acrylates are known to cross react.⁵⁶ However this was not consistent in our study.

Palladium chloride, Potassium dichromate, 1,4-Butanediol dimethacrylate, BIS-MA, BIS-GMA, N,N-Dimethylaminoethyl methacrylate, 1,6-Hexanediol diacrylate, Methylmethacrylate, , Mercury, Cobalt chloride, Eugenol, N, N-dimethyl-4-toluidine, 2-Hydroxy-4-methoxy benzophenone and 2(2-hydroxy-5-methylphenyl) benzotriazol, 4-Tolyldiethanolamine and Methylhydroquinone were also positive in some patients.

In contrast to the results seen in dental patients, there are positivities to acrylates seen in the dental personnel. The reason for this difference is because uncured monomer acrylate are responsible for

ACD.^{18,22} Dental personnel regularly handle these substances during the curing process whereas patients have a very short contact period with the same as the monomers would already have been cured when placed in the mouth. Dental personnel are further at risk as the monomers acrylates can penetrate through normal latex gloves.^{18,22}

It has been reported that dental personnel with occupational hand dermatitis and acrylate sensitivity also frequently showed positivity to one or more of the standard series allergens for example, nickel, cobalt, palladium, fragrance and colophony. This was consistent with our results.

The most common acrylate allergens that have been reported are 2-HEMA and EGDMA. However, in our study there was only one positivity each for both allergens.

SUMMARY AND CONCLUSION

SUMMARY AND CONCLUSION

Patients undergoing dental therapy such as root canal treatment, orthodontic treatment, prosthodontic treatment and dental implants have dental materials placed in the oral cavity for extended periods of time. Examples of such treatments are dental fillings, braces, dentures and implanted teeth. Many of the substances used for these treatments are known to cause allergic contact dermatitis (ACD).

ACD in the oral cavity can manifest in various ways such as oral lichenoid lesions (OLLs), gingivostomatitis, cheilitis, burning mouth, lip/facial swelling or oral ulcers. Lichenoid skin eruptions and eczema are also known to occur. Although the oral mucosa is constantly exposed to a large number of potential allergens and irritants, it is worthwhile to assess whether these patients have a specific allergy to dental materials.

Dental personnel handling the raw materials used for dental products are also at risk of developing ACD. Dentists mainly use amalgams and composites as fillings for dental cavities. Dental amalgams are composed of a mixture of metals and it is usually an alloy of mercury, silver, tin, copper and other trace metals.¹⁵ All these are potential allergens to dental personnel and patients.

Dental composite resin is used to fill dental cavities. This composite resin has to undergo a curing process before it can be used. This curing process involves linking of acrylic monomers to form polymers. These monomers are mainly responsible for ACD.⁵³

To produce dental composite resin, the dental personnel mix the specific acrylates with benzoyl peroxide and induce a polymerization process. This dough is then hardened by using heat or light. If this hardening has to occur at room temperature the reaction needs an accelerator (activator). Certain other additives called inhibitors are used to prevent unintended spontaneous polymerization. In addition to acrylates, both accelerators and inhibitors can cause sensitization.²²

Unpolymerized material that remains back after the curing process can leach out and act as an allergen for dental patients but as the contact time is short, they are less prone to develop ACD. Acrylic dentures also require a similar curing process. Both dental personnel and patients are at risk for ACD to acrylates in dentures.²²

Acrylic monomers can penetrate surgical latex gloves so dental personnel are not protected from coming into contact with these substances and are at a higher risk of developing ACD. Special types of

gloves like 4H-gloves have been advised in these patients but they are not popular as these gloves are expensive and have a poor anatomical fit.²²

Our study focused on two groups of people. One group was patients with previous dental treatment that presented with complaints of oral lesions or skin lesions that appeared after the dental treatment. The other group was dental personnel who handle dental materials with complaints of hand dermatitis.

Since we suspected ACD, which is a type of delayed hypersensitivity reaction, we patch tested these two groups with Chemotechnique dental series. Readings were taken at 48, 72 and 96 hrs.

Most of the dental patients had amalgam fillings and most of them had oral lichenoid lesions (OLLs). The most common allergens were metals such as nickel, copper, gold, potassium and mercury. Mercury and copper are found in dental amalgam and there could be a relevance of the positive patch test findings in these patients. Nickel is a common sensitizer in the general population and its relevance in this study is uncertain. The patients who tested positive to gold were all females (who regularly wear gold jewelry) and none of these patients had any dental treatment with gold in the oral cavity so the relevance gold allergy was also uncertain in our study.

None of our patients tested positive to any of the acrylates. As patients come into contact with uncured monomer acrylics for very short periods of time, this lack of positivity is not relevant. Acrylic allergy in denture-wearers has been reported but none of our patients had history of wearing dentures.

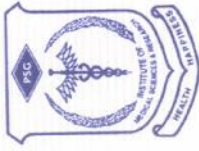
Studies have shown that removal of dental amalgams in patients with proven amalgam allergy has provided symptomatic relief with partial or complete healing of oral lesions. Other studies have shown relief of symptoms in patients even without showing sensitivity. This is postulated as a result of an irritant reaction to mercury vapors from the dental amalgam.¹⁵ None of our patients had their fillings removed so this correlation could not be assessed in our study.

Acrylic allergy in dental personnel is well documented. 5 out of 7 of the dental personnel tested in our study showed positivity to at least one acrylate. The most common acrylates which showed positivity in our study were BIS-GMA, BIS-MA and 1,4-Butanediol dimethacrylate. In one study it was suggested that 2-HEMA (2-hydroxyethyl methacrylate) and bis-GMA were enough to screen patients for acrylate allergy.

ACD to acrylates in dental personnel is difficult to manage as they cannot avoid coming into contact with these materials.

They can also be advised a replacement of treatment if found to be allergic to any of the constituents of their treatment. So if patients with amalgam fillings present with allergy, they can be advised for it to be changed to composite filling and vice versa.

Patch testing with dental series can be useful in patients with severe oral symptoms where there could be resolution of their complaints after removal of the offending agent. Patch testing is a simple, scientific and cost effective tool that can be used to detect contact allergies and to eliminate the offending agent and hence giving symptomatic relief to the patients.



Proposal Number

: 11/155

Project Title

Investigation of contact allergy to dental materials by patch testing with dental series

Investigator(s)

: Dr Swetha Sunny Kurian

Institution

: PSGIMS & R

Name of the Guide(s)

: Dr Reena Rai

Institution

: PSGIMS & R

Waiver of Consent

: No

Review Type

: Exempt

Date of the Meeting

: N/A

Decision

: Approved

Approval Date

: 09.01.2012

Validity of the Approval

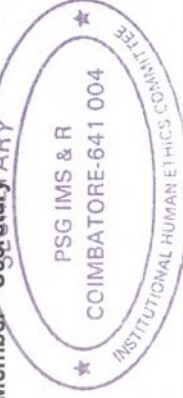
: One year

Approval for this study is given under the following terms and conditions:

1. Non-adherence to the Standard Operating Procedures (SOP) of the Institutional Human Ethics Committee (IHEC) and national and international ethical guidelines shall result in withdrawal of approval (suspension or termination of the study). SOP will be revised from time to time and revisions are applicable prospectively to ongoing studies approved prior to such revisions.
2. Pls are required to send progress reports (in the form of an extended abstract with publications if any) to the IHEC every six months (and a month before expiry of approval date, if renewal of approval is being sought).
3. Request for renewal must be made at least a month ahead of the expiry of validity along with a copy of the progress report.

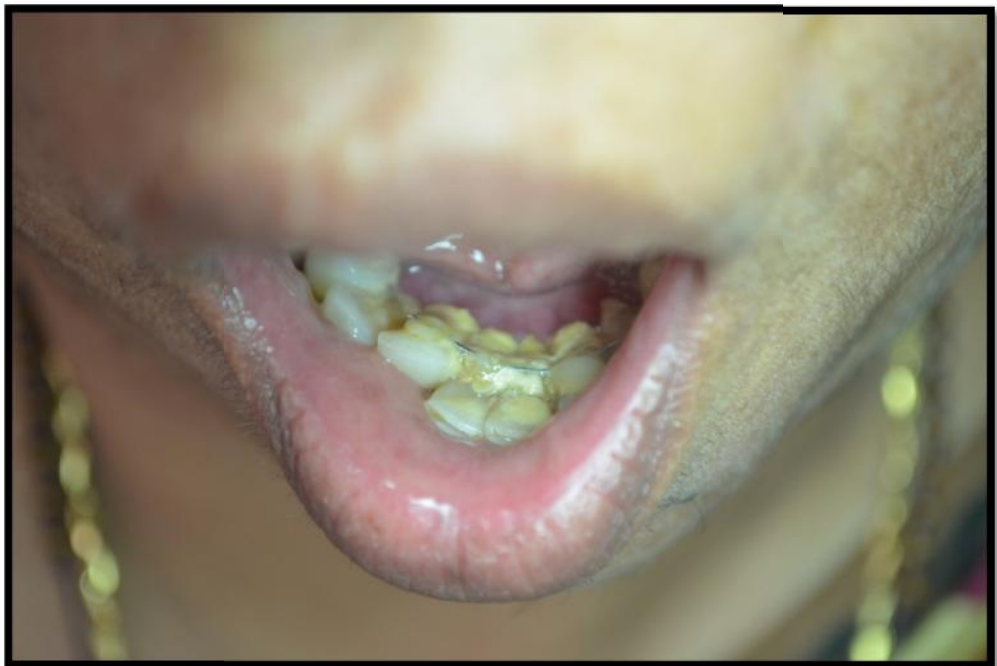
Dr Y S Sivan

Member-Secretary

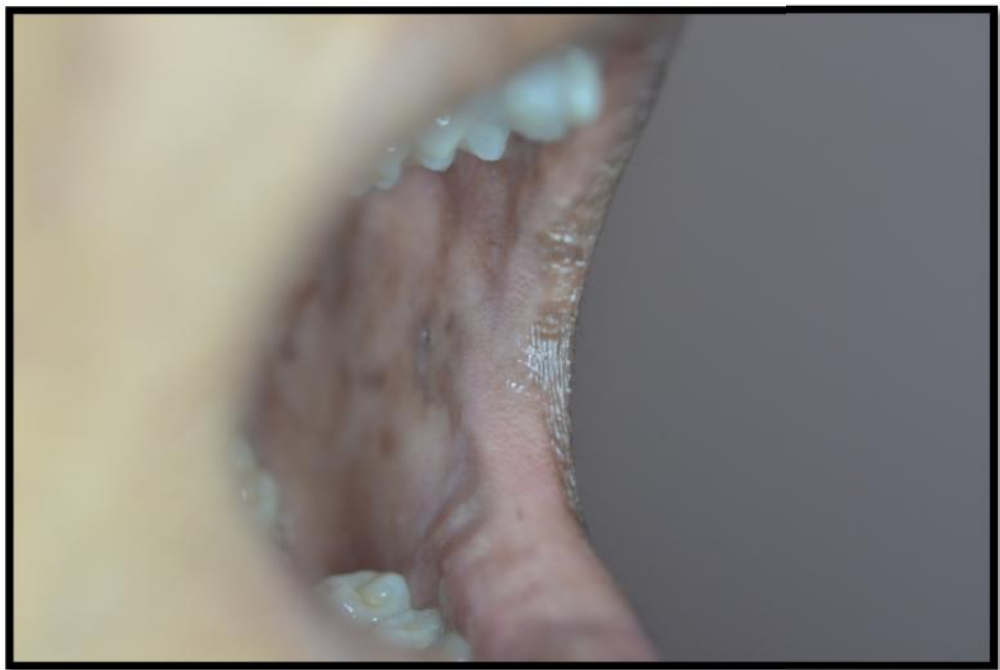




Picture 1. Amalgam filling



Picture 2. Dental wiring



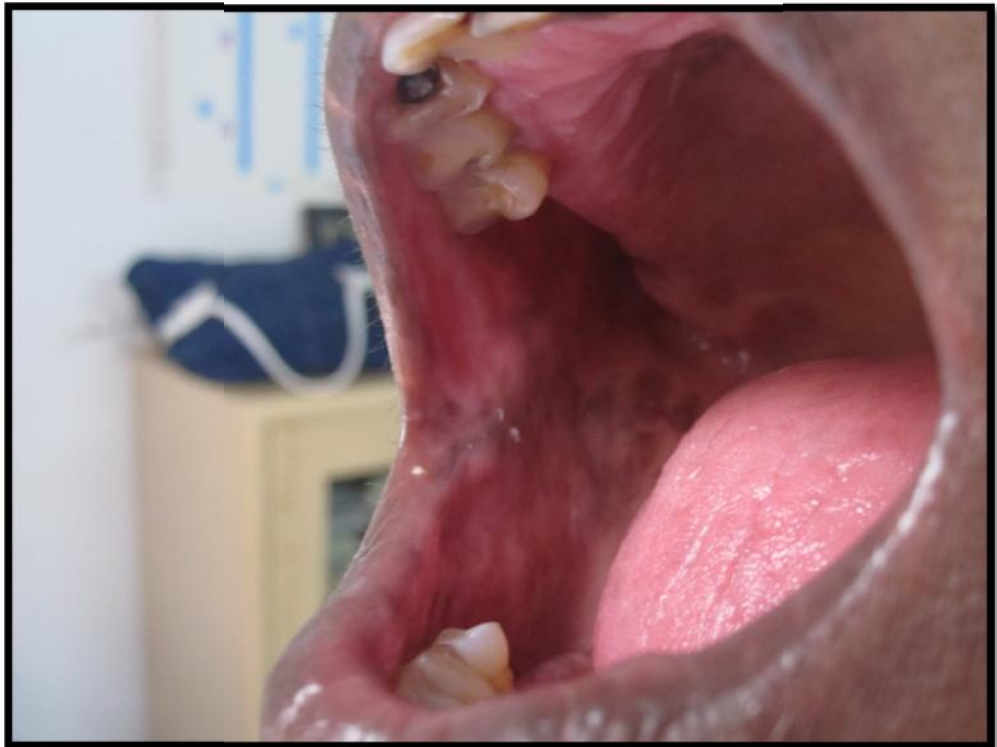
Picture 3. OLL buccal mucosa



Picture 4. OLL buccal mucosa



Picture 5. OLL on palate



Picture 6. OLL buccal mucosa with amalgam filling



Picture 7. OLL lower lip



Picture 8. Hand dermatitis with scaling of fingertips in a dental post graduate working with acrylic monomers



Picture 9. Hand dermatitis with post inflammatory depigmentation of right index fingertip in a dental post graduate working with acrylic monomers



Picture 10. Preparing the patient's back



Picture 13. Loaded Finn chambers ready to be applied



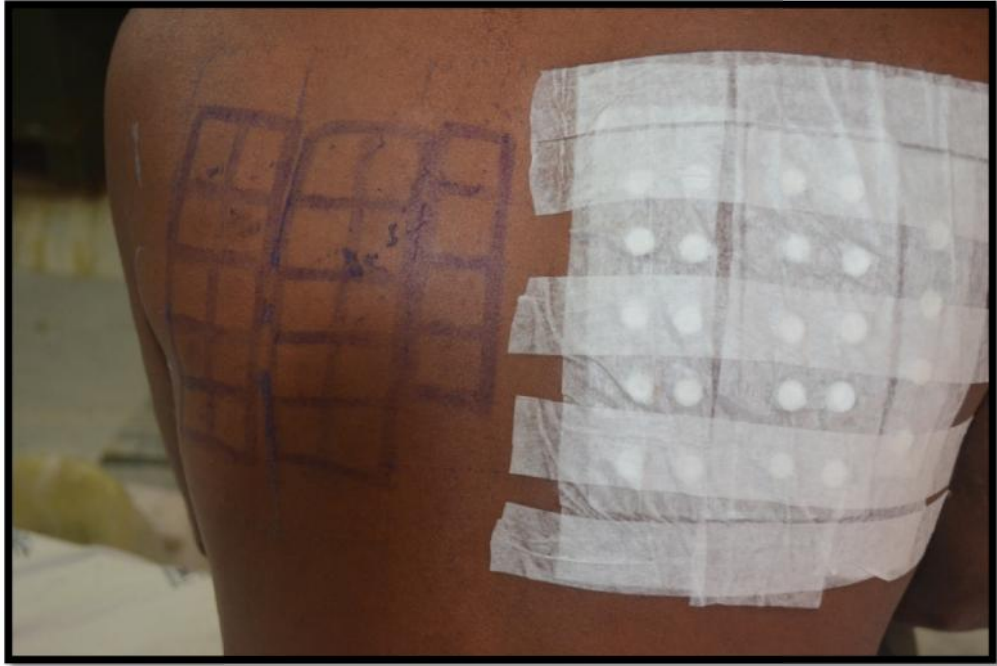
Picture 14. Technique for holding the tape



Picture 15. Application of Scanpor tape with loaded Finn chambers onto patient's back.



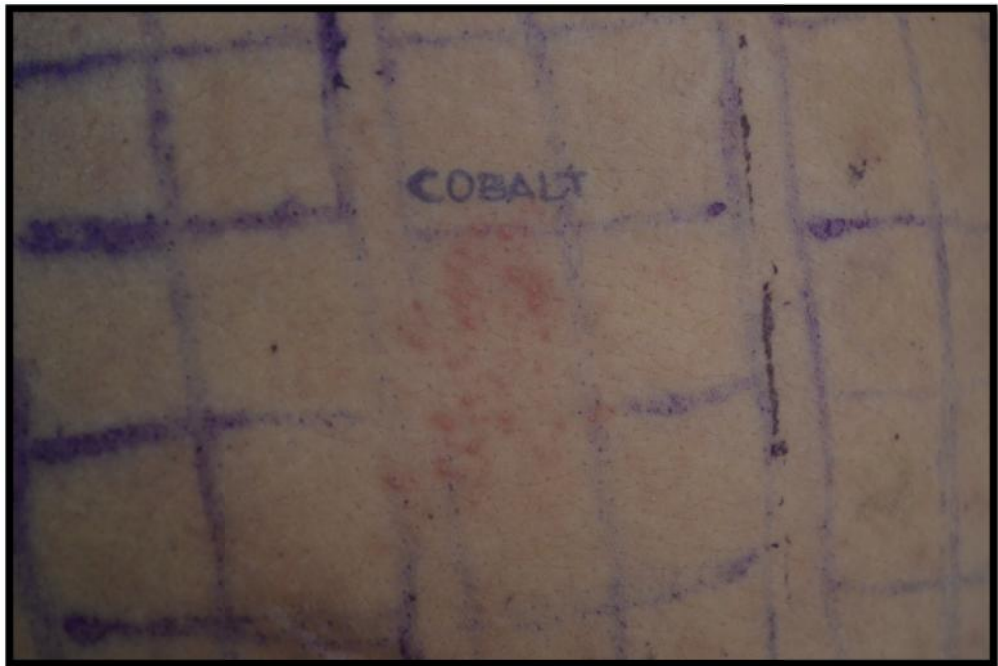
Picture 16. Patient with strips of Scanpor tapes secured with additional micropore tapes



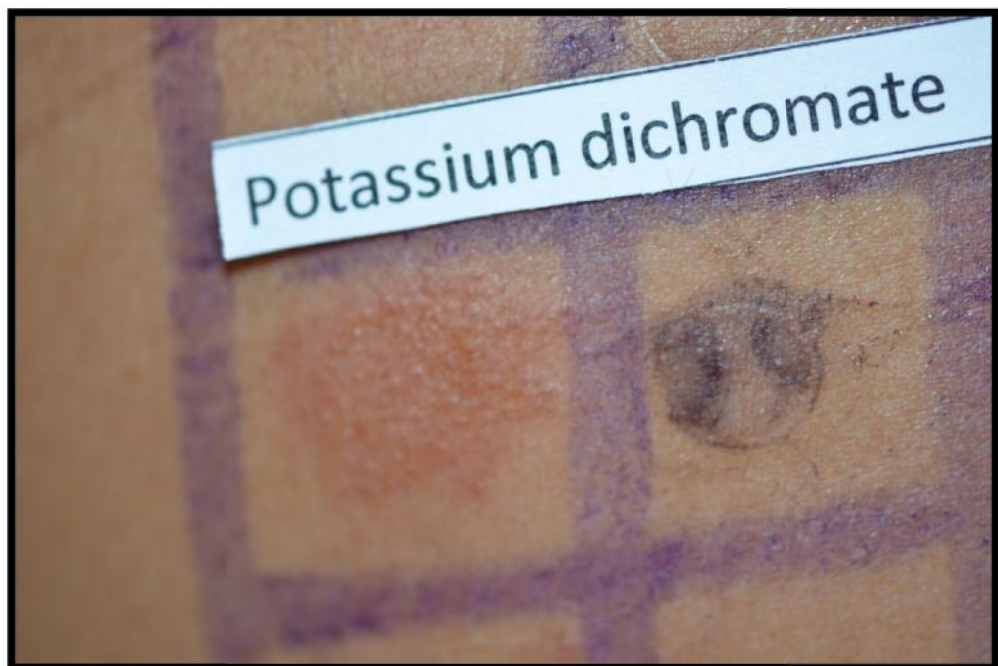
Picture 17. Back of the patient at 48 hours marked with gentian violet before taking the reading



Picture 18. Patch test positivity to cobalt in a patient with burning mouth and OLL



Picture 19. Patch test positivity to cobalt in a patient with burning mouth and OLL



Picture 20. Patch test positivity to Potassium dichromate



Picture 21. Patch test positivity to Gold sodium thiosulfate



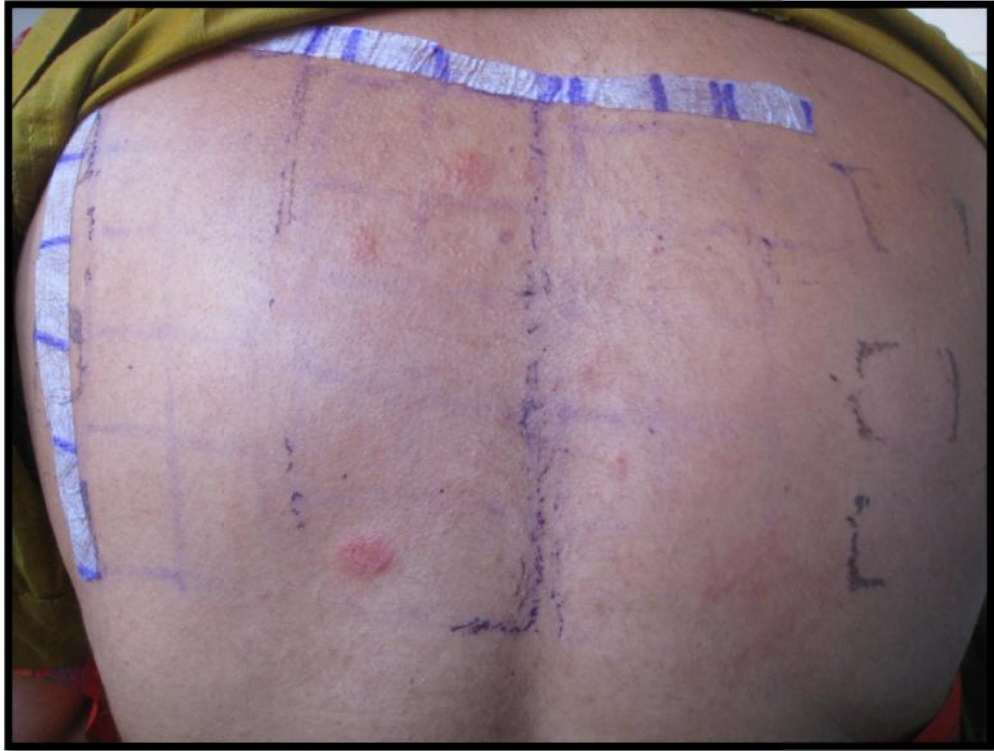
Picture 22. Patch test positivity to Gold sodium thiosulfate



Picture 23. Patch test positivity to Nickel sulfate



Picture 24. Multiple positivities in a dental student working with acrylic monomers



Picture 25. Multiple positivities in a patient with OLL



Picture 26. Single positivity in a dental patient

MASTER CHART - PATIENTS 1

Serial number	Demography				Type of Dental Treatment						Clinical Presentations						
	Name	Age	Sex	Hospital Number	Amalgam filling	Ceramic filling	Dental wiring	Dental Prostheses	Metal Crown	Ceramic Crown	Gingivitis	Stomatitis	Burning mouth	Oral Licheoid Lesions	Lip/Face swelling	Lichenoid eruptions elsewhere	Oral Ulcers
1	Vimala	55	F	I6021321	Y				Y	Y			Y	Y			
2	Indira	47	F	I2025681	Y							Y	Y				Y
3	Nandhini	24	F	O7049110	Y									Y			
4	Vasanthi	46	F	O12018725			Y	Y						Y			
5	Saminathan	49	M	O1022362	Y								Y				
6	Sujatha	31	F	O6023264	Y										Y		
7	Durai	32	M	O12018965	Y						Y	Y	Y	Y			Y
8	Srivenkatesan	46	M	O06034631	Y					Y			Y	Y			
9	Healthin Geetha	45	F	O60245621	Y								Y				Y
10	Abdullah	20	M	O12074978	Y				Y	Y			Y	Y			
11	Prema	55	F	O0626541	Y	Y							Y	Y			Y
12	Ponnuthai	60	F	O12065546			Y							Y			
13	Thangaraj	41	M	O7062512	Y												Y
14	Roseline Mary	52	F	O12086541	Y									Y			
15	Padmavathy	43	F	O8123654	Y									Y		Y	
16	Shanthi	37	F	I1452152				Y								Y	
17	Saroja	49	F	O6124861	Y									Y		Y	

MASTER CHART - DENTAL PERSONNEL 1

	Demography			Clinical presentation								Acrylates											
Serial number	Name	Age	Sex			Burning of hands	Itching of hands	erythema of hands	Scaling of hands	Blistering	Hyperpigmentation		8 1,4-Butanediol dimethacrylate	9 BIS-MA	13 2-Hydroxyethyl methacrylate	26 N,N-Dimethylaminoethyl methacrylate	27 1,6-Hexanediol diacrylate	29 Tetrahydrofurfuryl methacrylate	1.Methylmethacrylate	2.Triethyleneglycol dimethacrylate	3. Urethane dimethacrylate	4. Ethyleneglycol dimethacrylate	5. BIS-GMA
1	Anju	20	F				Y																
2	Vijayapriya	21	F					Y									P						
3	Divya	20	F						Y					P									
4	Divyabharathi	20	F		Y											P							
5	Niranjana	24	F				Y						P	P									P
6	Geetha	34	F				Y		Y	Y			P		P				P			P	P
7	Menaka	25	F				Y	Y	Y														
													2	2	1	1	1	0	1	0	0	1	2



Patch Testing - Dental Series - Proforma

Date:

Personal details

Name :

Age :

Address :

OP No. :

IP No. :

Sex :

Occupation :

Dental procedure

Date of Treatment

Details:

Complaints- Duration

a) Stomatitis / Gingivostomatitis

b) Burning / tingling month

c) Chelitis

d) Oral lichenoid lesions

e) Lip swelling / Face swelling

f) Redness

G) Any other complaint

Dental Personnel

Hand dermatitis -(Itching, Erythema, Scaling, fissuring)

Any other complaints

Duration of complaint

Type of dental materials in contact with

Patch test reading

D2

optimal

D4

D7

D10

Interpretation of Result

DENTAL SERIES

S.NO	ANTIGEN	%	DAY 2	DAY		
				4	7	10
01	Control					
02	Methyl methacrylate	2				
03	Triethyleneglycol dimethacrylate	2				
04	Urethane dimethacrylate	2				
05	Ethleneglycol dimethacrylate	2				
06	BIS-GMA	2				
07	N, N-dimethyl-4-toluidine	5				
08	2-Hydroxy-4-methoxy benzophenone	10				
09	1,4-Butanediol dimetharylate	2				
10	BIS-MA	2				
11	Potassium dichromate	0.5				
12	Mercury	0.5				
13	Cobalt chloride	1				
14	2-Hydroxyethyl mehacrylate	2				
15	Goldsodiumthiosulfate	2				
16	Nickel sulphate	5				
17	Eugenol	2				
18	Colophony	20				
19	N-Ethyl-4-toluenesulfonamide	0.1				
20	Formaldehyde	1				
21	4-Tolydiethanolamine	2				
22	Copper sulfate	2				
23	Methylhydroquinone	1				
24	Palladium chloride	2				
25	Aluminium chloride hexahydrate	2				
26	Camphoroquinone	1				
27	N,N-aDimethylaminoethyl methacrylate	0.2				
28	1,6-Hexanediol diacrylate	0.1				
29	2(2-hydroxy-5-methylphenyl) benzotriazol	1				
30	Tetrahydrofurfuryl methacrylate	2				
31	Tin	50				

PATCH TESTING CONSENT FORM

I, the undersigned, do hereby consent for undergoing
PATCH TESTING.

I confirm that the details of the procedure, its side effects
and benefits have been explained to me in a language that I
understand. I have been given the opportunity to clarify any
concerns that I have and sign this consent form freely and
voluntarily.

I give my full consent for all of the aforementioned.

Name : _____

Signature : _____

Xg;gjy; gotk;

..... Mfpa ehd;/ ngl;R ghpl;ir bra;J
bfhs;s rk;kjpf;fpnwd;. ,e;j ghpl;iriag; gw;wpa bray;Kiw
kw;Wk; gf;f tpist[fs; midj;Jk; vdf;F ehd; g[hpe;J bfhs;sf;Toa
bkhHpapy; kUj;Jth;fshy; tpsf;fg;gl;IJ. ,e;j ghpl;iria bra;J
bfhs;s ehd; KG rk;kjk; mspf;fpnwd;.

ifbahg;gk; :

bgah; :

njjp :

BIBLIOGRAPHY

- 1) Gawkrödger DJ. Investigation of reactions to dental materials. *Br J Dermatol*. 2005 Sep;153(3):479.
- 2) Raap U, Stiesch M, Reh H, Kapp A, Werfel T. Investigation of contact allergy to dental metals in 206 patients. *Contact Dermatitis*. 2009 Jun;60(6):339-43.
- 3) Bharti R, Wadhwani KK, Tikku AP, Chandra A. Dental amalgam: An update. *J Conserv Dent*. 2010 Oct;13(4):204-8.
- 4) Contact stomatitis and cheilitis. In: Rietschel RL and Fowler JF Jr, editors. *Fisher's Contact Dermatitis*. 6th ed. Ontario: BC Decker Inc; 2008. p. 700-721
- 5) Kanerva L, Estlander T, Jolanki R et al. Dermatitis from acrylates in dental personnel. In: Menné T and Maibach HI, editors. *Hand eczema*. Boca Raton: CRC Press; 1994. p. 231-254
- 6) Kanerva L, Rantanen T, Aalto-Korte K, Estlander T, Hannuksela M, Harvima RJ, et al. A multicenter study of patch test reactions with dental screening series. *Am J Contact Dermat*. 2001 Jun;12(2):83-7.
- 7) Bakula A, Lugović-Mihić L, Situm M, Turčin J, Sinković A. Contact allergy in the mouth: diversity of clinical presentations and diagnosis of common allergens relevant to dental practice. *Acta Clin Croat*. 2011 Dec;50(4):553-61.
- 8) Ahlgren C, Bruze M, Möller H, Gruvberger B, Axéll T, Liedholm R, Nilner K. Contact allergy to gold in patients with oral lichen lesions. *Acta Derm Venereol*. 2012 Mar;92(2):138-43.

- 9) Ditrichova D, Kapralova S, Tichy M, Ticha V, Dobesova J, Justova E, Eber M, Pirek P. Oral lichenoid lesions and allergy to dental materials. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2007 Dec;151(2):333-9.
- 10) Drucker AM, Pratt MD. Acrylate contact allergy: patient characteristics and evaluation of screening allergens. Dermatitis. 2011 Apr;22(2):98-101.
- 11) Torgerson RR, Davis MD, Bruce AJ, Farmer SA, Rogers RS 3rd. Contact allergy in oral disease. J Am Acad Dermatol. 2007 Aug;57(2):315-21.
- 12) Waroquier D, Evrard L, Nelis M, Parent D. Allergic contact stomatitis presenting as geographical tongue with pruritus. Contact Dermatitis. 2009 Feb;60(2):106.
- 13) Dunsche A, Kästel I, Terheyden H, Springer IN, Christophers E, Brasch J. Oral lichenoid reactions associated with amalgam: improvement after amalgam removal. Br J Dermatol. 2003 Jan;148(1):70-6.
- 14) Sockanathan S, Setterfield J, Wakelin S. Oral lichenoid reaction due to chromate/cobalt in dental prosthesis. Contact Dermatitis. 2003 Jun;48(6):342-3.
- 15) McParland H, Warnakulasuriya S. Oral lichenoid contact lesions to mercury and dental amalgam--a review. J Biomed Biotechnol. 2012.

- 16) Dutrée-Meulenberg RO, Kozel MM, van Joost T. Burning mouth syndrome: a possible etiologic role for local contact hypersensitivity. *J Am Acad Dermatol*. 1992 Jun;26(6):935-40.
- 17) Eisen D, Eisenberg E. Oral lichen planus and the burning mouth syndrome. Is there a role for patch testing? *Am J Contact Dermat*. 2000 Jun;11(2):111-4.
- 18) Sasseville D. Acrylates. *Dermatitis*. 2012 Jan;23(1):3-5.
- 19) Björkner B, Frick-Engfeldt M, Pontén A, et al. Plastic materials. In: Johansen JD, Frosch P, Lepoittevin JP, editors. *Contact Dermatitis*. 5th edition. Berlin: Springer; 2011. p. 695-723.
- 20) Malten KE, den Arend JA, Wiggers RE. Delayed irritation: hexanediol diacrylate and butanediol diacrylate. *Contact Dermatitis*. 1979 May;5(3):178-84.
- 21) Calnan CD. Cyanoacrylate dermatitis. *Contact Dermatitis*. 1979 May;5(3):165-7.
- 22) Kanerva L, Estlander T, Jolanki R. Occupational skin allergy in the dental profession. *Dermatol Clin*. 1994 Jul;12(3):517-32.
- 23) Farli M, Gasperini M, Francalanci S, Gola M, Sertoli A. Occupational contact dermatitis in 2 dental technicians. *Contact Dermatitis*. 1990 May;22(5):282-7.
- 24) Riva F, Pigatto PD, Altomare GF, Riboldi A. Sensitization to dental acrylic compounds. *Contact Dermatitis*. 1984 Apr;10(4):245.

- 25) Nethercott JR, Jakubovic HR, Pilger C, Smith JW. Allergic contact dermatitis due to urethane acrylate in ultraviolet cured inks. *Br J Ind Med*. 1983 Aug;40(3):241-50.
- 26) Goon AT, Isaksson M, Zimerson E, Goh CL, Bruze M. Contact allergy to (meth)acrylates in the dental series in southern Sweden: simultaneous positive patch test reaction patterns and possible screening allergens. *Contact Dermatitis*. 2006 Oct;55(4):219-26.
- 27) Santosh V, Ranjith K, Shenoi SD, Sachin V, Balachandran C. Results of patch testing with dental materials. *Contact Dermatitis*. 1999 Jan;40(1):50-1.
- 28) Fisher AA. In: *Contact Dermatitis*. 3rd edition. Philadelphia: Lea and Febiger; 1986
- 29) Metals. In: Rietschel RL and Fowler JF Jr, editors. *Fisher's Contact Dermatitis*. 6th ed. Ontario: BC Decker Inc; 2008. p. 641-699
- 30) Fisher AA. Allergic sensitization of the skin and oral mucosa to acrylic denture materials. *J Am Med Assoc*. 1954 Sep 18;156(3):238-42.
- 31) Crissey JT. Stomatitis, dermatitis, and denture materials. *Arch Dermatol*. 1965 Jul;92(1):45-8.
- 32) Bowen RL. Compatibility of various materials with oral tissues. I: The components in composite restorations. *J Dent Res*. 1979 May;58(5):1493-503.

- 33) Ruyter IE, Svendsen SA. Remaining methacrylate groups in composite restorative materials. *Acta Odontol Scand.* 1978;36(2):75-82.
- 34) Tosti A, Bardazzi F, Piancastelli E, Brasile GP. Contact stomatitis due to N,N-dimethyl-para-toluidine. *Contact Dermatitis.* 1990 Feb;22(2):113.
- 35) Kaaber S, Thulin H, Nielsen E. Skin sensitivity to denture base materials in the burning mouth syndrome. *Contact Dermatitis.* 1979 Mar;5(2):90-6.
- 36) O'Driscoll JB, Beck MB, Kessler ME, Ford G. Contact sensitivity to aluminium acetate eardrops. *Contact Dermatitis.* 1991 Feb;24(2):156-7.
- 37) Warshaw EM, Belsito DV, DeLeo VA, Fowler JF Jr, Maibach HI, Marks JG, et al. North American Contact Dermatitis Group patch-test results, 2003-2004 study period. *Dermatitis.* 2008 May-Jun;19(3):129-36.
- 38) Fowler J Jr, Taylor J, Storrs F, Sherertz E, Rietschel R, Pratt M et al. Gold allergy in North America. *Am J Contact Dermat.* 2001 Mar;12(1):3
- 39) Nedorost S, Wagman A. Positive patch-test reactions to gold: patients' perception of relevance and the role of titanium dioxide in cosmetics. *Dermatitis.* 2005 Jun;16(2):67
- 40) Koch P, Bahmer FA. Oral lesions and symptoms related to metals used in dental restorations: a clinical, allergological, and histologic study. *J Am Acad Dermatol.* 1999 Sep;41(3 Pt 1):422

- 41) Scalf LA, Fowler JF Jr, Morgan KW, Looney SW. Dental metal allergy in patients with oral, cutaneous, and genital lichenoid reactions. *Am J Contact Dermat*. 2001 Sep;12(3):146
- 42) Yiannias JA, el-Azhary RA, Hand JH, Pakzad SY, Rogers RS 3rd. Relevant contact sensitivities in patients with the diagnosis of oral lichen planus. *J Am Acad Dermatol*. 2000 Feb;42(2 Pt 1):177-82.
- 43) Ahnlide I, Ahlgren C, Björkner B, Bruze M, Lundh T, Möller H, et al. Gold concentration in blood in relation to the number of gold restorations and contact allergy to gold. *Acta Odontol Scand*. 2002 Oct;60(5):301-5.
- 44) Goossens A, De Swerd A, De Coninck K, Snauwaert JE, Dedeurwaerder M, De Bonte M. Allergic contact granuloma due to palladium following ear piercing. *Contact Dermatitis*. 2006 Dec;55(6):338-41.
- 45) Faurschou A, Menné T, Johansen JD, Thyssen JP. Metal allergen of the 21st century--a review on exposure, epidemiology and clinical manifestations of palladium allergy. *Contact Dermatitis*. 2011 Apr;64(4):185-95.
- 46) Frykholm KO, Frithiof L, Fernström AI, Moberger G, Blohm SG, Björn E. Allergy to copper derived from dental alloys as a possible cause of oral lesions of lichen planus. *Acta Derm Venereol*. 1969;49(3):268-81.
- 47) López-Lerma I, Vilaplana J, Romaguera C. Intraoral contact allergy to camphoroquinone. *Contact Dermatitis*. 2008 Dec;59(6):377-8. doi: 10.1111/j.1600-0536.2008.01323.x.

- 48) Torres V, Mano-Azul AC, Correia T, Soares AP. Allergic contact cheilitis and stomatitis from hydroquinone in an acrylic dental prosthesis. *Contact Dermatitis*. 1993 Aug;29(2):102-3.
- 49) Raap U, Stiesch M, Kapp A. Contact allergy to dental materials. *J Dtsch Dermatol Ges*. 2012 Jun;10(6):391-6.
- 50) Laeijendecker R, Dekker SK, Burger PM, Mulder PG, Van Joost T, Neumann MH. Oral lichen planus and allergy to dental amalgam restorations. *Arch Dermatol*. 2004 Dec;140(12):1434-8.
- 51) Khamaysi Z, Bergman R, Weltfriend S. Positive patch test reactions to allergens of the dental series and the relation to the clinical presentations. *Contact Dermatitis*. 2006 Oct;55(4):216-8.
- 52) Rustemeyer T, Frosch PJ. Occupational skin diseases in dental laboratory technicians. (I). Clinical picture and causative factors. *Contact Dermatitis*. 1996 Feb;34(2):125-33.
- 53) Medications and medical devices, and implications for the medical community. In: Rietschel RL and Fowler JF Jr, editors. *Fisher's Contact Dermatitis*. 6th ed. Ontario: BC Decker Inc; 2008. p. 125-174
- 54) Bruze M, Björkner B, Lepoittevin JP. Occupational allergic contact dermatitis from ethyl cyanoacrylate. *Contact Dermatitis*. 1995 Mar;32(3):156-9.
- 55) Henriks-Eckerman ML, Kanerva L. Gas chromatographic and mass spectrometric purity analysis of acrylates and methacrylates used as patch test substances. *Am J Contact Dermat*. 1997 Mar;8(1):20-3.

- 56) Goon AT, Bruze M, Zimerson E, Sörensen Ö, Goh CL, Koh DS, Isaksson M. Variation in allergen content over time of acrylates/methacrylates in patch test preparations. *Br J Dermatol*. 2011 Jan;164(1):116-24.
- 57) Practical aspect of patch testing. In: Rietschel RL and Fowler JF Jr, editors. *Fisher's Contact Dermatitis*. 6th ed. Ontario: BC Decker Inc; 2008. p. 11-29
- 58) van Loon LA, van Elsas PW, van Joost T, Davidson CL. Contact stomatitis and dermatitis to nickel and palladium. *Contact Dermatitis*. 1984 Nov;11(5):294-7.
- 59) Foussereau J, Laugier P. Allergic eczemas from metallic foreign bodies. *Trans St Johns Hosp Dermatol Soc*. 1966;52(2):220-5.
- 60) Fisher AA, Shapiro AA. Allergic eczematous contact dermatitis due to metallic nickel. *J Am Med Assoc*. 1956 Jun 23;161(8):717-21.
- 61) Wilson HT. Nickel dermatitis. *Practitioner*. 1956 Sep;177(1059):303-8.
- 62) Laine J, Kalimo K, Happonen RP. Contact allergy to dental restorative materials in patients with oral lichenoid lesions. *Contact Dermatitis*. 1997 Mar;36(3):141-6.
- 63) Basko-Pluska JL, Thyssen JP, Schalock PC. Cutaneous and systemic hypersensitivity reactions to metallic implants. *Dermatitis*. 2011 Apr;22(2):65-79.

- 64) Downs AM, Sansom JE. Colophony allergy: a review. *Contact Dermatitis*. 1999 Dec;41(6):305-10.
- 65) Lewis BB, Chestner SB. Formaldehyde in dentistry: a review of mutagenic and carcinogenic potential. *J Am Dent Assoc*. 1981 Sep;103(3):429-34.